POLYISOBUTYLENE AS A POLYMER SUPPORT FOR HOMOGENEOUS CATALYSIS

A Dissertation

by

CHAYANANT HONGFA

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

December 2008

Major Subject: Chemistry

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Approved by:

Chair of Committee,	David E. Bergbreiter
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ABSTRACT

Polyisobutylene as a Polymer Support for Homogeneous Catalysis.

(December 2008)

Chayanant Hongfa, B.S., Pennsylvania State University

Chair of Advisory Committee: Dr. David E. Bergbreiter

Phase selective soluble polymers are useful in organic synthesis because they simplify purification and separation processes. Such selective soluble polymers enable the use of Green chemistry principles to be utilized as ways to simplify catalyst, reagent, and product recovery. Polyisobutylene oligomers serve as examples of such polymers. Vinyl terminated polyisobutylene (PIB) oligomers can be easily transformed into a variety of end-functionalized PIB oligomers. Previous work has shown that PIB oligomers possess nonpolar phase selective solubility that allows them to be used as polymer supports for ligands and catalysts in liquid/liquid biphasic systems. This dissertation focuses on the use of PIB oligomers as supports for a salen Cr(III) complex, a Hoveyda-Grubbs 2nd generation catalyst, and a *N*-heterocyclic carbene. The syntheses of these PIB-supported ligands and catalysts are simple and straightforward. The synthetic products and the intermediates in these syntheses can all be readily analyzed and monitored by conventional spectroscopic methods. The activity of the PIB-supported catalysts is shown to be analogous to that of other soluble polymer supported catalysts or their non-supported analogs. The PIB-bound catalysts can be separated from

products by a latent biphasic, liquid/liquid extractions, or product self-separation systems. The recovered PIB-bound catalysts can then be recycled multiple times.

DEDICATION

To my mom and dad for all of their love and support over the years. To Cindy, without you things would have turned out a lot differently.

ACKNOWLEDGEMENTS

I would like to give my sincere and deepest thanks to Professor Bergbreiter for being such a great teacher and mentor. His unique methods of guidance and tutelage have taught me how to become not just a chemist, but a true research scientist. I will always remember him for his passion for chemistry and his love of teaching it.

I would like to thank Professor Kociolek for his advice when I was lost as a junior back at Penn State. Professor Kociolek inspired me to be a chemist. The opportunity to work in his research lab was a privilege. I would have never pursued my Ph.D. without his support and guidance.

I would like to express my gratitude to the members of Bergbreiter's group. First, I would like to acknowledge Dr. Furyk for his help as my mentor in my early years as a graduate student in Bergbreiter's group. Toward the end of my second year, I would like to give thanks to Dr. Hamilton for his support as my second mentor. I would also like to acknowledge Dr. Tian for our long discussions about PIB; without him a lot of my projects would not have worked. I would like to thank two of my mentees, Chris and Dominique. I would also like to thank Dr. Ortiz-Acosta, Dr. Sung, Dr. Liao, Su, Hui, Jeff, Dr. Koizumi, and Jill for being my friends and colleagues throughout my experience as a graduate student at Texas A&M University.

I would also like to give a special thanks to Dr. Thomas (Jackie). Without her support and our long study sessions together, I would have never made it through

graduate school. Thanks for being such a great friend and colleague throughout five years of my life as a graduate student at Texas A&M University.

I would also like to express my thanks to Hanshi Montoya and all of his students at Montoya Shorin Kempo Karate. Hanshi helped me through many of my tough spots throughout my career as a graduate student at Texas A&M. My training at the dojo was my refuge. The friendships of my fellow students encouraged me and without them my life in graduate school would have been a lot harder to bear.

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CHAPTER I

INTRODUCTION*

New catalysis research over the last century has led to the widespread use of catalysts in fine chemical processes. However the high cost of precious metals, the cost of the ligands, the potential problems of product contamination by catalyst residues, and the increasing interest in Green Chemistry has led to increasing interest in ways to recover and recycle catalysts. Industrial processes that employ catalysts can use either homogeneous or heterogeneous catalysts. Heterogeneous catalysts can be easily recycled by simple filtration after the reaction is over. Heterogeneous catalysts though often have modest catalytic selectivity and less reactive than homogeneous catalysts. Homogeneous catalysts are generally as reactive, but can be more selective than heterogeneous catalysts because homogeneous catalysts' activity can be tuned by varying ligand structure. However, the solubility of homogeneous catalysts makes separation of these catalysts from their products more problematic.

One of the strategies developed to address the problems of catalyst recovery and separation from products was to use insoluble polymers as supports for the catalyst. Polymers were first introduced as supports for organic synthesis by Merrifield and Letsinger who used cross-linked polystyrene for solid-phase syntheses of peptides and

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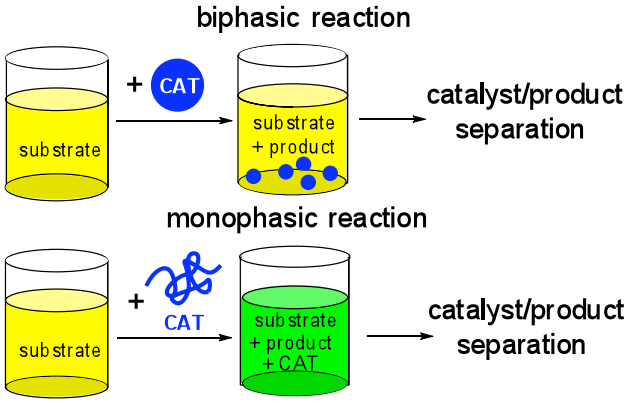
nucleotides.[1,2] This discovery revolutionalized the field of organic syntheses by introducing the use of cross-linked polymers in solid phase synthesis. The same separation strategies used in this body of work have also been employed for use in homogeneous catalysis. The interest in this topic is extensive and there are many reviews on the topic of using insoluble polymers as supports for ligands and catalysts.[3-6] However, in spite of this body of work, successful and practical strategies for homogeneous catalysis recovery, separation, and reuse remain elusive. Thus alternative approaches where soluble polymers are used as supports and then separated after the reaction have received increasing attention in recent years.[3,7-10]

A key difference between a strategy that uses an insoluble cross-linked polymer and a strategy that uses a soluble polymer is that the latter strategy allows a catalytic reaction to be carried out under homogeneous conditions. In most cases where a cross-linked polymer is used to support a catalyst, the catalyst is necessarily separated from products before, during, and after the reaction because it is attached to an insoluble support. In the case of soluble polymers, the phase separation event can occur after the reaction. This phase separation can employ a permselective membrane, a solid/liquid separation after selective polymer precipitation, or a liquid/liquid separation of two different density liquid phases containing either a catalyst or product, respectively. The most common separation processes use solid/liquid or liquid/liquid separations. These processes are contrasted in Scheme 1. Processes that use soluble polymer-supported catalysts that are separable, recoverable and reusable after a reaction by a latent biphasic, liquid/liquid extractions, and product self-separation systems are the focus of this dissertation. In the

following, I have briefly discussed some historical and some more recent examples of others' work that has used various sorts of soluble polymers as supports for ligands and catalysts. This discussion first focuses on various polymer supports such as poly(ethylene glycol), non-cross-linked polystyrene, polynorbornene, and polyethylene, where the recovery of a catalyst is effected by a solid/liquid separation. Subsequently, I have briefly discussed examples of polymer-bound catalysts that are separable after a reaction by different liquid/liquid separations such as water/organic biphasic systems, thermoregulated phase transfer catalysis, aqueous biphasic catalysts separable by extraction, organic/organic biphasic systems, thermomorphic phase selectively soluble polymers, and latent biphasic separations.

Scheme 1. Strategic differences between use of an insoluble cross-linked polymer supported catalyst and a soluble polymer supported catalyst.



Solid/Liquid Separation of Soluble Polymer-Bound Ligands and Catalysts

Solid/liquid separation is the general approach used to separate products from catalysts bound cross-linked polymers and or to separate products and reagents or catalysts that are immobilized on inorganic supports. This is the scheme most others have used with soluble polymer-bound transition metal catalysts. Most commonly separation only requires a filtration. In cases where the solids that form are not readily filtered, centrifugation is often effective in separating a solid from solution.

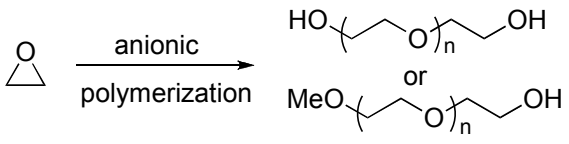
The techniques of filtration or centrifugation are simple and carrying out a solid/liquid separation of a soluble polymer-bound catalyst after a homogeneous reaction has also been used to separate catalysts from products. In the case of soluble polymers, a phase perturbation that induces the polymer-supported species to separate as a solid is required to precipitate the polymer-bound catalyst. This can involve a temperature change as described below for thermomorphic systems. In this case no significant additions of solvent are required, and the separation can be carried out under reaction conditions. More commonly, a solid/liquid separation of a polymer-supported species from a product solution is effected by changing the solvent to one in which the polymer is not soluble. The significant additions of solvent required in solvent precipitation may be a problem in large scale processes. Nonetheless, solvent precipitation is the most general way to carry out a solid/liquid separation of a soluble polymer-bound catalyst and product after a homogeneous catalytic reaction. In either thermomorphic or solvent precipitation schemes, it is assumed that the products remain in solution.

Poly(ethylene glycol) (PEG)-Bound Ligands and Catalysts

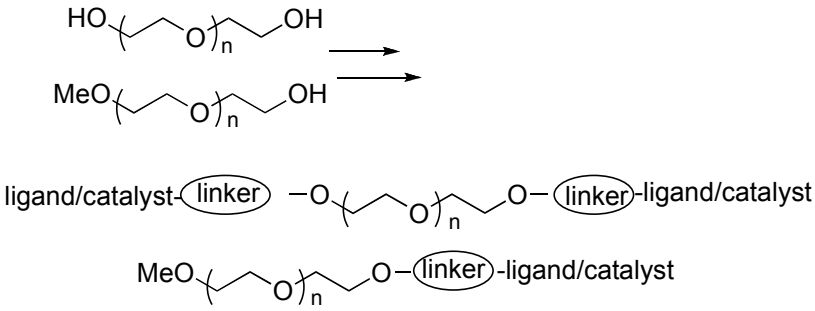
Poly(ethylene glycol) (PEG) is a linear polymer formed from the polymerization of ethylene oxide. Along with polystyrene, it was one of the first soluble polymers used to facilitate catalysis and synthesis.[8,11-13] PEG is a smaller version of poly(ethylene oxide) (PEO), a polymer with a $–CH_2CH_2O-$ repeating unit. PEG is the form of this polymer used in synthesis and catalysis because PEGs are polyethers with molecular weights of less than 20,000. With up to two terminal functional groups, polymers of this size have functional group loadings of at least 0.1 mmol/g. These polyether supports are most commonly recovered by solvent precipitation and filtration. PEG is insoluble in hexane, diethyl ether, *tert*-butylmethyl ether (TBME), isopropyl alcohol, and cold ethanol. These are the solvents usually used for the precipitation process.[14] PEG is usefully soluble in a wide range of solvents including DMF, dichloromethane, toluene, CH_3CN, and water. This broad solubility facilitates the use of PEG-supported species under homogeneous reaction conditions. As a soluble linear polymer with a simple repeating unit that only obscures a small part of a typical ^{1}H-NMR spectrum, the structure and loading of end groups can often be analyzed by solution-state ^{1}H-NMR spectroscopy.

The commercial availability of many PEG derivatives with either two $-CH_2OH$ end groups or one $-CH_2OH$ end group makes it easy to prepare a variety of PEG supported ligands and catalysts. In addition, more complex functional derivatives of PEG are commercially available. If desired, PEG polymers can be prepared by anionic polymerization of ethylene oxide.[15] The free hydroxyl groups on the polymers that are purchased or prepared by eq. 1 can be modified by simple organic reactions to form

ligands or catalysts (eq. 2). In the absence of branching, loading of ligands or catalysts is limited to one (-OCH_3, -OH termini) or two (two -OH termini) equivalents of ligand or catalyst per mole of polymer. Linkers as shown in eq. 2 are not required but are sometimes used.



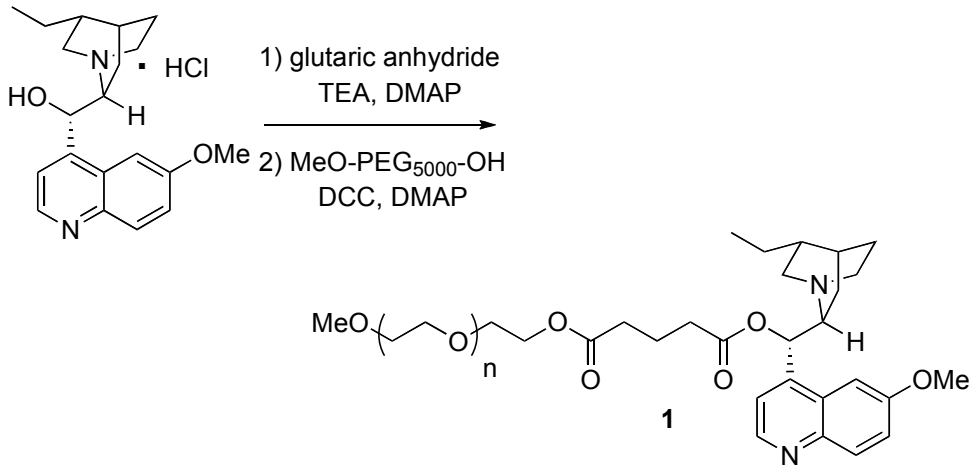
(1)



(2)

The Sharpless osmium-catalyzed asymmetric dihydroxylation reaction possesses great synthetic utility, and many efforts have been directed toward the development of polymer-supported *Cinchona* alkaloid ligands for this reaction.[8] The first example of a soluble polymeric support for *Cinchona* alkaloid was reported by Janda in 1996.[16] Janda's group attached MeO-PEG_{5000} through a glutarate linker to dihydroquinidine (DHQD) via the chiral secondary alcohol of the alkaloid to afford PEG-bound DHQD **1** as shown in eq. 3. This PEG-bound *Cinchona* alkaloid **1** was used in the Sharpless asymmetric dihydroxylation of *trans*-stilbene using *N*-methylmorpholine *N*-oxide (NMO) as the stoichiometric oxidant and led to a product diol that had 88% ee. Ligand

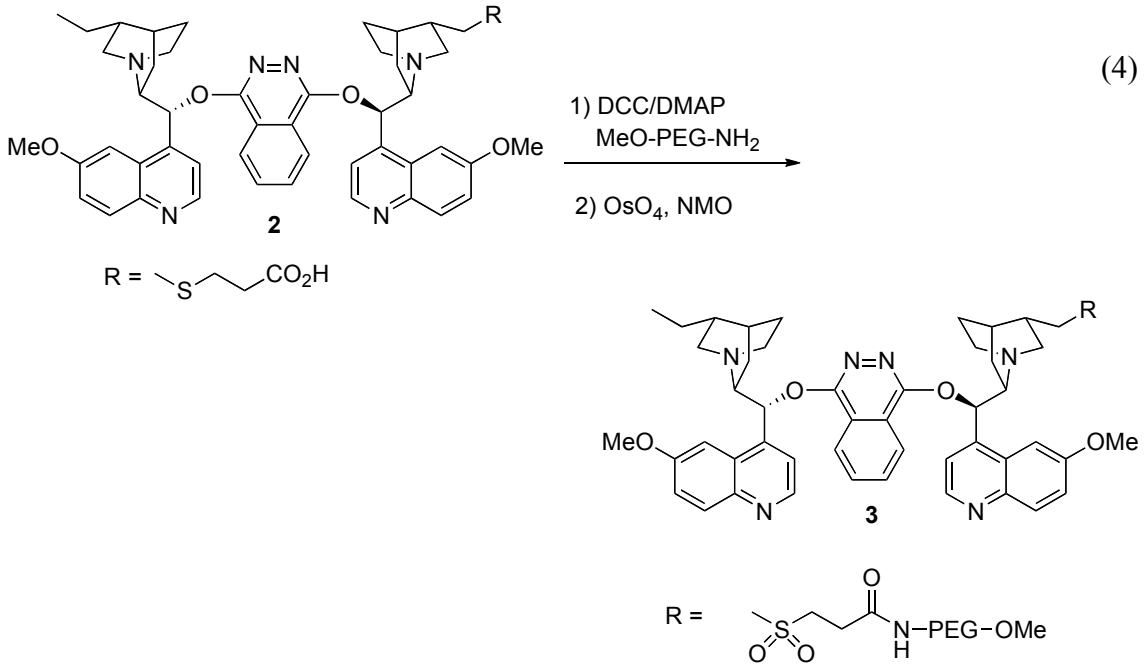
1 was recovered by solvent precipitation and reused five times with no apparent loss of reactivity.



(3)

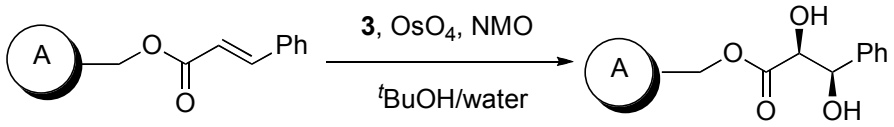
This initial report of describing PEG-bound *Cinchona* alkaloid ligands by Janda's group was successful in providing the advantage of insoluble polymer supports while at the same time affording the reactivity and selectivity advantages of a soluble polymer. However, in this study, the reactivity and selectivity of the catalytic reaction using the PEG-bound *Cinchona* alkaloid ligand **1** was still not as high as seen for a low molecular weight counterpart. In order to improve on their initial work, Janda's group developed a second-generation PEG-bound *Cinchona* alkaloid **3**.[17] This PEG-modified phthalazine ligand **3** was synthesized from MeO-PEG-NH_2 and DHQD derivative **2.** PEG-bound *Cinchona* alkaloid **3** was found to be soluble in both *tert*-butyl alcohol/water and acetone/water mixtures. This PEG-bound *Cinchona* alkaloid ligand **3** was effectively used in Sharpless asymmetric dihydroxylation of *trans*-stilbene with either NMO or

K_3FeCN_6 as penultimate oxidants and led to diol products with 94% ee and 99% ee respectively. These results were a major improvement in reactivity and selectivity of over those seen using ligand **1.**



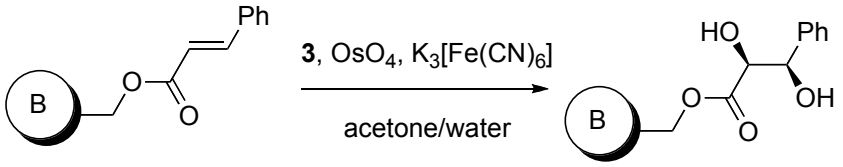
(4)

Janda's group demonstrated how a chiral ligand could be integrated onto a soluble polymeric species so that ligand-accelerated catalysis such as Sharpless asymmetric dihydroxylation can operate in an unhindered manner. With this success, Janda expanded his studies to include the case in which a small organic moiety is attached to a polymeric matrix.[18] In order to accomplish this goal, Janda's group took advantage of their previous work and use PEG-bound *Cinchona* alkaloid **3** to perform multipolymer asymmetric dihydroxylation reactions on various species of polymer bound olefins as shown in eq. 5-7. The use of NMO as a penultimate oxidant in *tert*-butyl alcohol/water



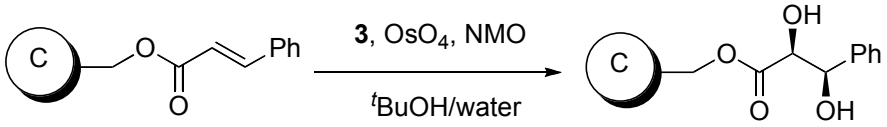
(5)

4a



(6)

4b



(7)

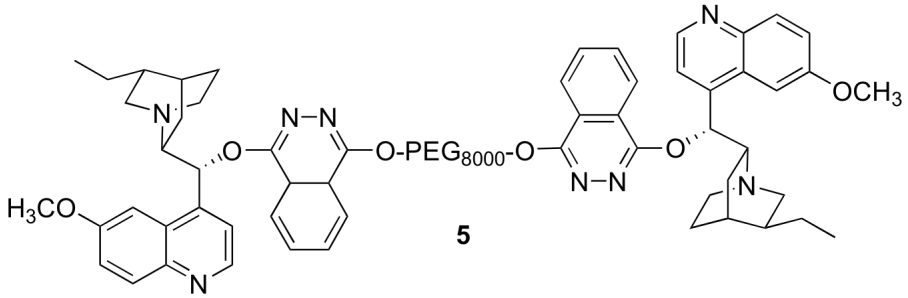
4c

A = Tentagel (lightly crosslinked polymer)
B = Wang or Merrifield resin (porous highly crosslinked polymer)
C = PEG (linear, soluble polymer)

worked well for Tentagel and PEG supported *trans*-cinnamates **4a** and **4c**, while $K_3[Fe(CN)_6]$ in acetone/water was needed for Wang and Merrifield resin supported *trans*-cinnamates **4b**.

Janda's work described above showed that PEG-bound *Cinchona* alkaloids and their derivatives are useful as chiral ligands for Sharpless asymmetric alkene dihydroxylation. PEG-bound *Cinchona* alkaloid and its derivatives are also widely used for aminohydroxylation reactions.[19] Xu and Lin recently described using PEG 4000, 6000, and 8000 immobilized *Cinchona* alkaloid ligands for the catalytic asymmetric aminohydroxylation of alkenes using $K_2OsO_2(OH)_4$ as a catalyst and AcNHBr as a

nitrogen source.[20] In this case, the *Cinchona* alkaloid was first converted to a monosubstituted chlorophthalazine using 1,4-dichlorophthalazine. Then the dilithium salt of a PEG diol was inserted to form the PEG derivative **5**. This PEG derivative **5** was then used in an asymmetric aminohydroxylation reaction. Various derivatives of *trans*-cinnamate were examined as substrates (eq. 8). The products' ee values were in the range of 74-99% ee and the regioselectivity of the aminohydroxylation was >10:1. The polymeric ligand **5** formed using PEG_{8000} was recovered by solvent precipitation and was

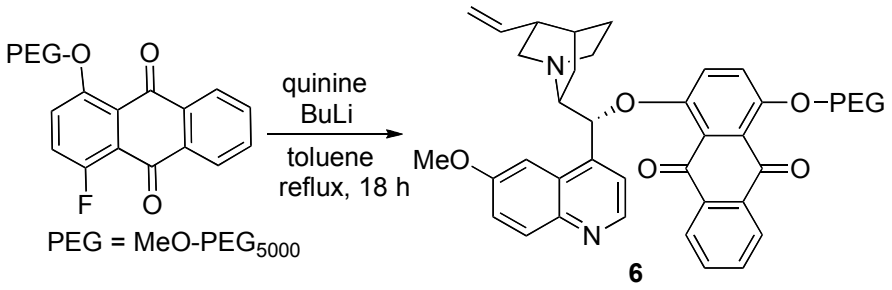


(8)

reused with isopropyl *trans*-cinnamate with yields of ca. 90% and >95% ee in each of 5 cycles

In 2005, Zhang described immobilization of *Cinchona* alkaloids with an anthraquinone core onto PEG_{5000} (eq. 9).[21] This PEG-bound *Cinchona* alkaloid **6** was used in asymmetric dihydroxylation with various alkenes with high stereoselectivities (>80% ee) and high yield (>80%). The PEG-bound *Cinchona* alkaloid **6** was recovered

by solvent precipitation with diethyl ether and recycled through five cycles with *p*-chlorostyrene as a substrate. The average yield of all 5 cycles was 93% with the minimum stereoselectivity of 96% ee.

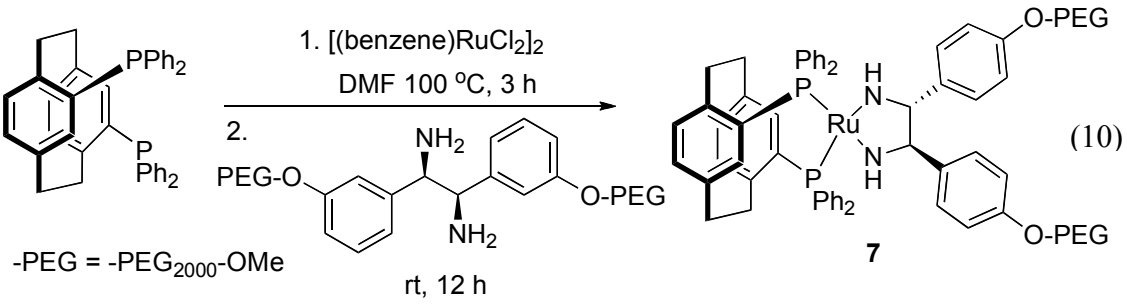


(9)

As noted above, PEG can be used to support other catalysts in addition to chiral ligands for Os-catalyzed reactions, PEG's broader utility is illustrated in some other select examples of asymmetric catalysis described below.

Optically active 1,2-diphenylethylenediamine (DPEN) is a useful chiral ligand and DPEN or its derivatives have been used as ligands for metals to generate highly enantioselective catalysts for many asymmetric organic transformations.[22] In 2003, Xiao's group described a synthesis of a PEG-supported DPEN Ru(II) complex **7** (eq. 10) that was in turn used for asymmetric hydrogenation of ketones (eq. 11).[23] This PEG-DPEN-bound Ru(II) complex was effective in reduction of various aromatic ketones to alcohols with high conversion (>98%) and high stereoselectivity (>90% ee). For example, complex **7** was used to reduce 1- or 2-acetonaphthone, various *p*-substituted acetophenones and propiophenone to the corresponding benzylic alcohols in greater than 95% yield with greater than 95% ee. Catalyst recovery was reported and variously

involved precipitation with diethyl ether or removal of solvents and extraction of the catalyst residue by diethyl ether. The diethyl ether insoluble catalyst that was recovered was reused three times without any change in the yield or stereoselectivity for reductions like those in eq. 16. Analysis for Ru leaching showed 2.7 ppm Ru in the diethyl ether washes – a concentration that could represent as much as 5-10% of the charged Ru.



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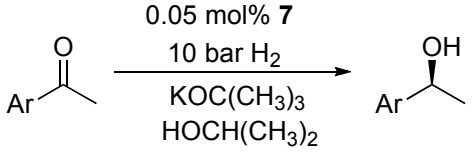
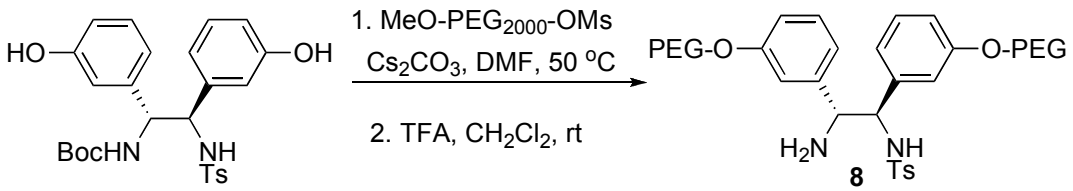


(11)

In subsequent work, a monotosylamide of a dihydroxylated DPEN was immobilized onto PEG_{2000} (eq.12) and the resulting PEG-bound species **8** was used as a ligand for Ru(II) in asymmetric transfer hydrogenation of aromatic ketones with ammonium formate as a hydrogen source (eq. 13).[24] While high conversions (66-100%) and high ee's (87-95%) were seen in the first cycle, the conversions dropped to 56% and the ee dropped to 82% in the third cycle. Although ICP-MS analysis of the solution phase showed < 0.7% of the ruthenium was lost by leaching, the stability of the ruthenium complexes was thought to be a possible problem affecting recycling.



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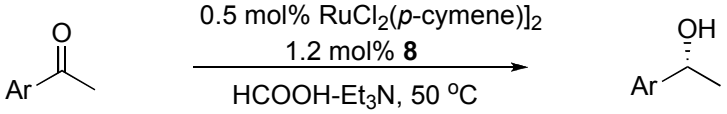
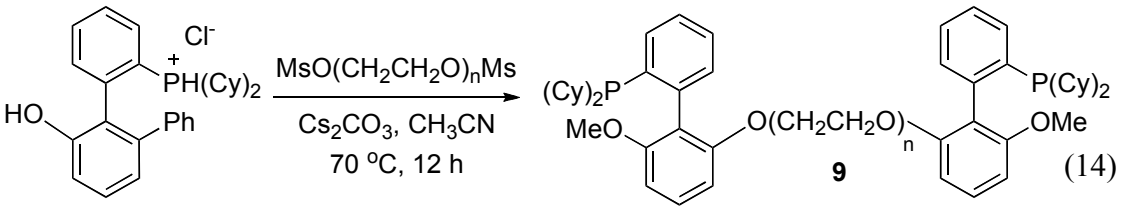


(13)

As noted above, PEG was one of the first polymer supports used in catalysis and PEG-bound phosphines were among the first soluble polymeric ligands. Since those initial reports in the 1960s,[13] many other supported phosphines have been prepared. More recently interests have shifted to developing chemistry to support chiral phosphine ligands for asymmetric catalysis. A report by Garcia's group of a PEG-supported SPhos phosphine that was used for Pd-catalyzed couplings of aryl chlorides is illustrative of this current interest.[25] In this case, a PEG-bound SPhos **9** derivative was prepared using the chemistry in eq. 14 and was tested both in the Buchwald-Hartwig amination of aryl halides with secondary amines (eq. 15) and in Suzuki couplings (eq. 16) . In this case, the authors compared this PEG-bound SPhos **9** with SPhos on a soluble non-cross-linked polystyrene support, a cross-linked polystyrene support and SPhos on SiO_2. In aryl amination of 2,5-dimethylchlorobenzene by morpholine, Pd ligated by **9** was the most reactive SPhos Pd catalyst with a TOF that was ca. 60-fold greater than that of a similar ligated Pd catalyst on cross-linked polystyrene and >1000-fold more reactive than a similar catalyst bound to SiO_2. In Suzuki coupling of 2,6-dimethylchlorobenzene and 2-

methylphenylboronic acid, Pd ligated by **9** was also the most reactive and the SPhos Pd catalyst had a TOF that was 20-fold larger than that of a similar ligated Pd catalyst on SiO_2.



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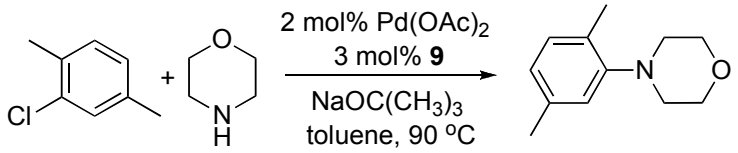

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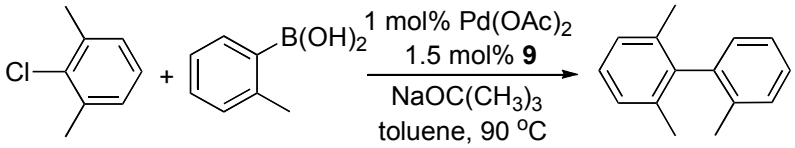


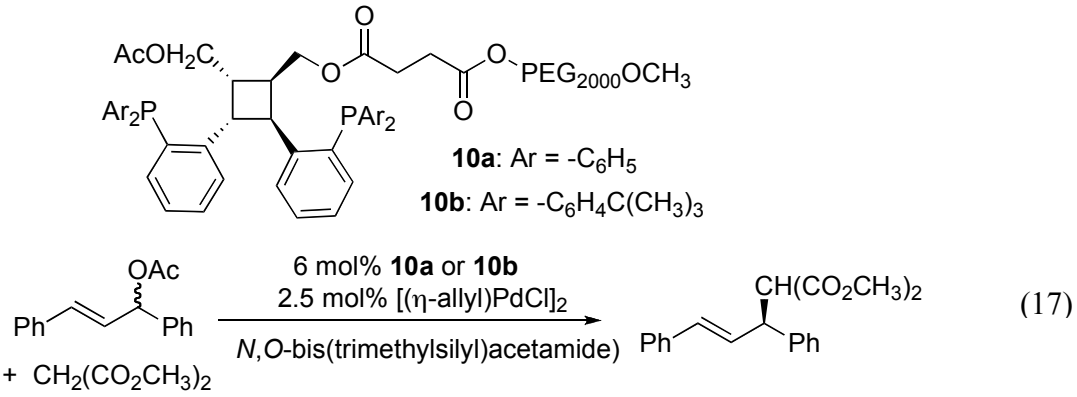
(16)

The PEG-bound SPhos **9** was recycled through eight cycles for the Buchwald-Hartwig amination reactions with a more reactive substrate like 4-chloroacetophenone but both in this case and other attempted recycling studies, notable decreases in yield and increases in reaction times were observed. While these phosphines are reportedly less sensitive to oxidation than other phosphines,[26] the general problem of phosphine oxidation that others have seen in Pd-catalyzed chemistry[27] remains a problem with **9**. This is evidenced by the results in this case where these authors found that based on ^{31}P-NMR spectroscopy, the recovered PEG-supported ligands **9** were highly oxidized after

the reaction. A further problem was that the conditions required for regeneration of the oxidized version of **9** by reduction detached the SPhos from the polymer.

Chiral bisphosphine ligands on a cyclobutane backbone that were developed by Ding's group for asymmetric allylic alkylation have been successfully attached to a PEG_{2000} polymer via a succinate linker.[28] In this chemistry, the PEG_{2000} group served several functions. While the main purpose of the polymer was to recover a Pd catalyst, the PEG_{2000} also facilitated purification of the ligands during the synthesis. That chemistry used a dicyclohexylcarbodiimide and DMAP as reagents to couple the half acid formed from MeO-PEG_{2000}-OH and succinic anhydride to a one or the other enantiomer of a bisphosphine on a cyclobutane that had been previously resolved. This ester synthesis generated the desired products **10a** and **10b** along with unreacted starting material and dicyclohexylurea (DCU). While the DCU was insoluble in the CH_2Cl_2 solvent used in the esterification, the separation of the bisphosphine from starting materials might have, for example, required a column chromatography which would have possible exposed the phosphines to oxygen and led to undesired phosphine oxides. In this case, this was avoided by evaporating the solvent from the solution of starting material and the PEG-bound bisphosphine and then simply washing away any diethyl ether-soluble starting materials or byproducts form the diethyl ether insoluble PEG_{2000}-bound bisphosphine. Chiral bisphosphine ligands **10a** or **10b** so prepared contained either a bis(diphenylphosphinyl) or bis(4-*tert*-butyldiphenylphosphinyl) ligand and were successfully used to form a Pd-complex *in situ* using $(\eta\text{-allylPdCl})_2$ and then used in an asymmetric allylic alkylation using dimethyl malonate (eq. 17). Yields through 9 cycles

with 2.5 mol% of Pd and 6 mol% of ligand **10b** in eq. 17 varied from 99% (cycles 1-6) to 81% in cycle 9. Enantioselectivity was relatively constant at 91% ee ±3% through these 9 cycles.



(17)

Non-Cross-Linked Polystyrene (NCPS)-Bound Ligands and Catalysts

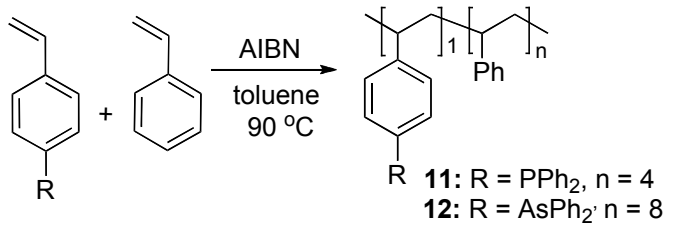
Polystyrene is an attractive linear soluble polymer to use for supporting catalysts because the chemistry used to immobilize ligands and catalysts mirrors that used on the more common cross-linked polystyrene supports – supports whose chemistry has been extensively explored because of their important role in peptide synthesis and combinatorial chemistry during the past 30 years.[13] In the case of linear polystyrenes, functionality to support ligands or catalysts can be introduced directly during a polymerization using an appropriate comonomer or post-polymerization by modification of the polymer. In many cases, a combination of steps is used. Control of the amount of functionality can be achieved by varying the amount of comonomer in a polymerization or by controlling reaction conditions in post-polymerization modification. Analyses of

the amount of functionality (ligand or catalyst) can often be carried out by solution-state ^{1}H-NMR spectroscopy though the background signals due to polystyrene's own NMR spectrum make some spectral regions essentially opaque. Polystyrene is usefully soluble in THF, dichloromethane, chloroform, benzene, and ethyl acetate. It is insoluble in hexane, methanol and water.[8] Its insolubility in select solvents means that the polystyrene-bound ligands or catalysts can be recovered and recycled by the same type of solvent precipitation process used for PEGs. When such a precipitation works, it allows one to separate the polymer and solution phase products by simple filtration. While non-cross-linked polystyrene-bound catalysts are typically been recovered by solvent precipitation, substituted polystyrenes can be recovered using a liquid-liquid separation too.[29]

Soluble polymer supported variants of triphenylphosphine like the PEG-supported phosphine ligands discussed above were among the earliest examples of soluble polymeric catalyst ligands.[13] Studies of these sorts of ligands and their close relative triarylarsines have continued into the present because these species are both versatile tools for organic synthesis and as useful ligands. Separable soluble polymer-bound versions of these species simplify product purifications and facilitate catalyst recycling.

In 2003, Toy reported a simple synthesis of 4-styryldiphenylphosphine and the radical copolymerization of it with styrene to form the polymeric phosphine **11** (eq. 18)**.** The ligand loading of **11** was determined by elemental analysis to be 1.5 mmol of PAr_3/g**.** The copolymer **11** was used successfully in Mitsunobu reactions with a 1.5-fold excess of the polymeric phosphine affording products in yields that ranged from 65-

83%.[30] Precipitation of **11** using cold diethyl ether separated the polystyrene-supported triarylphosphine from the product and, unlike the case with PPh_3, the use of **11** yielded products without any trace of phosphine or phosphine oxide contamination.



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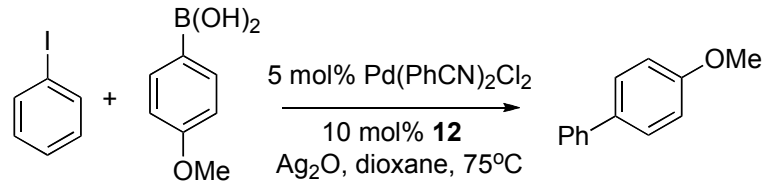
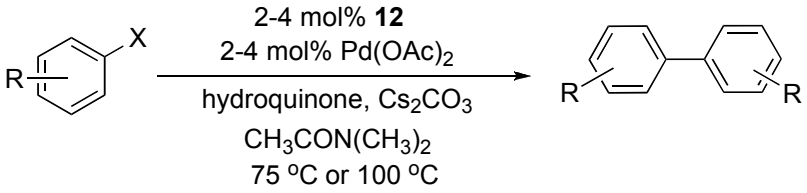
Toy's initial success led to the development of an NCPS-bound triarylarsine **12** from 4-diphenylarsinostyrene by a polymerization like that used to prepare **11** (eq. 18).[31] The ligand loading of **12** was determined by ^{1}H-NMR spectroscopy after the oxidation of **12** by hydrogen peroxide to be 0.83 mmol $AsAr_3$/g. The product copolymer **12** was then used as a ligand for Pd in Suzuki cross-coupling reactions (eq. 19**)**.[32] These reactions afforded products in yields of 84-88%, yields like those obtained using $AsPh_3$ as a ligand for Pd. The authors noted that at 75 °C, the refluxing temperature of 1,4-dioxane, the recovered **12** was not contaminated with Pd black, but that at 101 °C Pd black was formed. When the Pd catalysts formed with **12** were used at 75 °C, catalyst recycling by precipitation (MeOH) was feasible without any requirement for added Pd for four cycles.



(19)

In 2005, Toy described Pd-catalyzed homocoupling of aryl halides (R = -NO_2, -CH_3, -H, -OCH_3) using **12** (eq. 20).[33] An unhindered aryl iodide formed product in high yield (90%) but the reaction time more than doubled and the yields decreased to 80% with similar aryl bromides. More hindered aryl halides had even longer reaction times and formed products in yields that were below 50%. No recycling experiments were described in this study.



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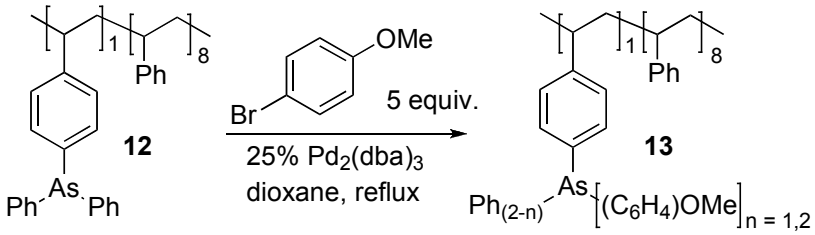
In 2007, Chiu used **12** as a ligand for Pd-catalyzed Stille coupling.[34] In this report, the authors first showed that these polymer-bound triarylarsines were effective ligands for Stille biaryl synthesis, ligands that were better than the corresponding phosphine ligand **11**. They also showed that recycling of Pd catalysts ligated by **12** was practical. However, in these studies they also noted that the product mixture in later cycles using **12** as the initial Pd ligand had progressively more of the desired 4-methoxybiphenyl product vis-à-vis the undesired biphenyl side product. They showed this was due to aryl

exchange of 4-bromoanisole with the polymeric arsine. This observation was then exploited to design a polymeric triarylarsine that would minimize biphenyl by-product formation. When they first treated **12** with 4-bromoanisole in the presence of $Pd_2(dba)_3$ they formed **13**, a version of **12** whose aryl groups are enriched with methoxyphenyl groups (eq. 21). When the polymer-bound triarylarsine **13** was used as a ligand in a Stille coupling of 4-bromoanisole with phenyltributyltin, the amount of biphenyl byproduct seen dropped to 15% (vs. 34% using **12**) (eq. 22). In this work, the NCPS-bound catalysts were recovered by concentrating the reaction mixture in THF and then using 20% diethyl ether in hexane to effect a precipitation of the NCPS-Pd complex.



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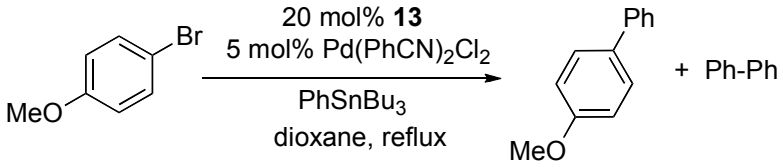

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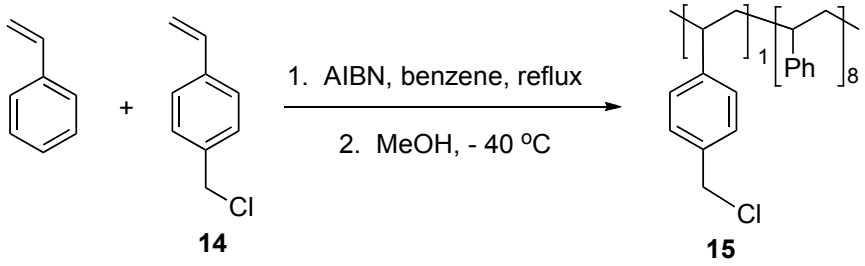
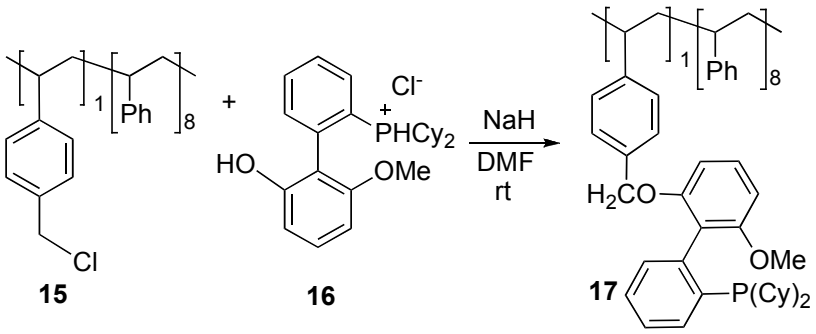
As noted above, Sphos phosphine is an extremely good ligand for amination and Suzuki coupling of sterically hindered aryl chlorides and it has been successfully attached to both PEG and NCPS by the García group. This group synthesized the functionalized NCPS **15** from the radical polymerization of styrene and 4-chloromethyl styrene **14** (eq. 23). NCPS-bound Sphos **17** was synthesized from the functionalized

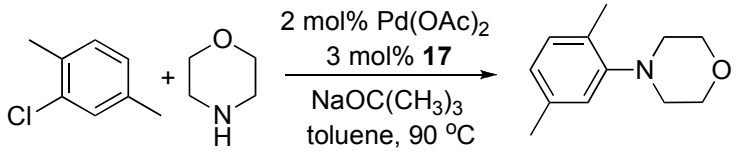
NCPS **15** and **16** as shown in eq. 24 and used the product ligand for Pd-catalyzed coupling chemistry of aryl chlorides (eq. 25-26).[25] As was true with PEG supports, Pd catalysts ligated by **17** were recoverable by solvent precipitation in cold diethyl ether. However, a Pd catalyst ligated by **17** was less reactive than its PEG analog and the reusability of the Pd catalysts was compromised by phosphine oxidation.



14 **15** (23)



15 **16** **17** (24)



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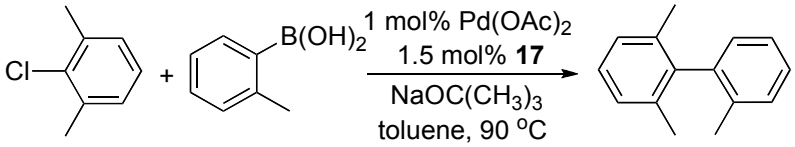
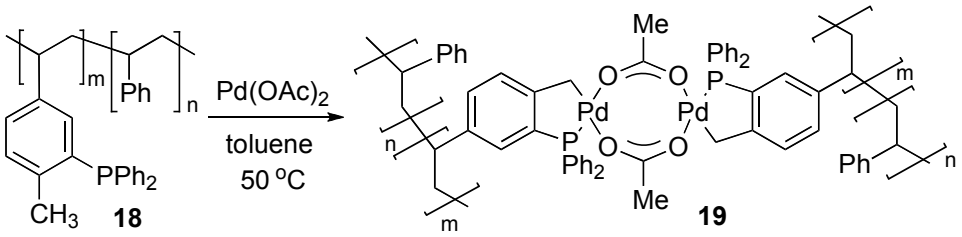


(26)

In 2005, Luo described using NCPS to support a palladacycle catalyst similar to one described earlier by Herrmann as being particularly effective for Heck and Suzuki reactions. This carboxylate-bridged palladacycle was attached either by copolymerization of a palladacycle-containing styrene monomer with styrene or by metalation of a preformed phosphine-containing polymer **18** (eq. 27).[35,36] This NCPS-bound Pd complex was then used in Heck and Suzuki chemistry (cf. eq. 28). The catalyst **19** was successfully recycled four times.



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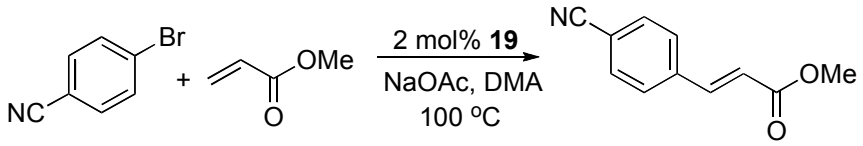

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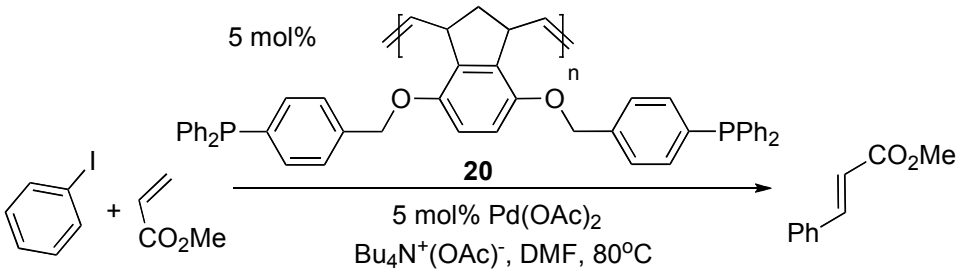
Polynorbornene-Supported Ligands and Catalysts

Ring-opening metathesis polymerization has provided chemists with a variety of soluble polymer supports that have been used to facilitate synthesis and catalysis.[37-39] Such supports are useful in the synthesis of libraries of compounds of biological interest.[40] These sorts of supports generally are prepared using a norbornene-containing

monomer. Two examples of these soluble polymer-bond catalysts are briefly discussed below.

Luh and Yang reported the synthesis of polynorbornene-supported phosphine ligands **20** that were useful in Pd-catalyzed cross coupling chemistry (eq. 29-31).[41] The Pd catalysts formed with these ligands were all competent in the first cycle with aryl iodides but the activity of the catalysts decreased cycle to cycle. In the case of the Heck coupling chemistry, the polymer-bound catalyst was soluble at 80 °C but was insoluble at room temperature. This thermomorphic system provided the most recyclable catalyst with the initial 95% yield dropping to 85% in the fifth cycle. Catalysts that were recovered using solvent precipitation generally had larger decreases in activity cycle to cycle.



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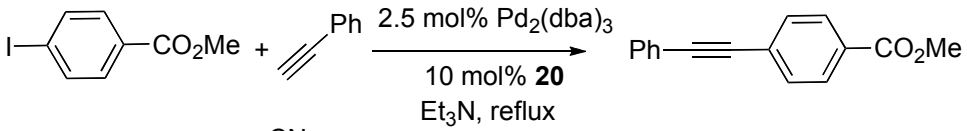

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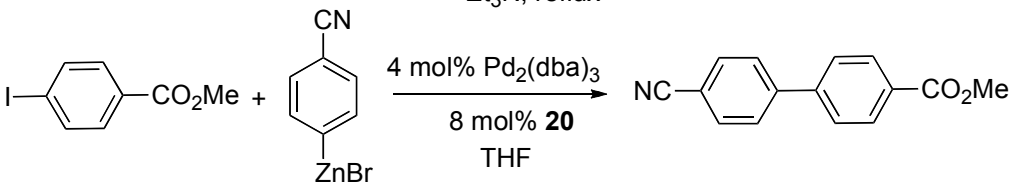
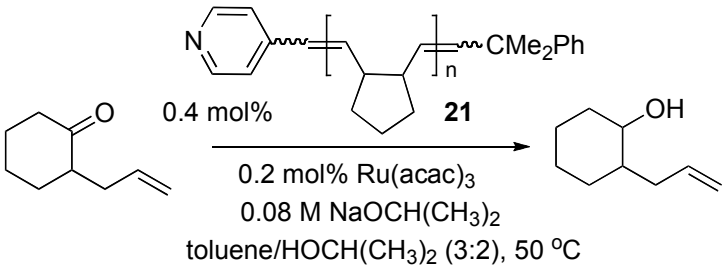


(31)

Nomura and Kuromatsu reported using polynorbornene as a soluble support for various pyridine and bipyridyl ligands that were used as ligands for Ru in selective hydrogen transfer reduction of ketones.[42] This polymeric ligand **21** was prepared by a living ring-opening metathesis polymerization using a Schrock type molybdenum-alkylidene initiator and the bipyridine or pyridine was introduced onto the product polymer by a Wittig-like reaction with an aldehyde-substituted pyridine derivative. When $Ru(acac)_3$ was added to an *i*-PrOH/toluene solution of these ligands in the presence of $NaOCH(CH_3)_2$, cyclohexanone was reduced to cyclohexanol with TONs of ca 250-300. Recycling was studied with the pyridine-terminated polymer **21**. TON values for cyclohexanone reduction decreased by less than 5% cycle to cycle. Similar results were seen for the reduction of allylcyclohexanone in eq. 32 where the first and second cycle TON values were both 125. The reduction of acetophenone as shown in eq. 33 was also studied with TON value of 141.



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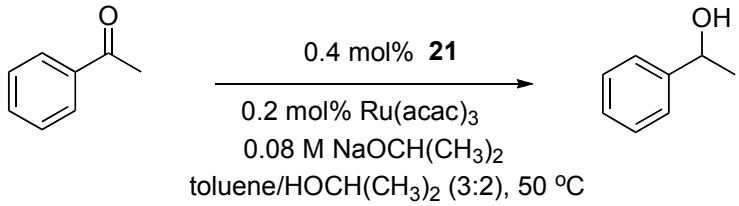

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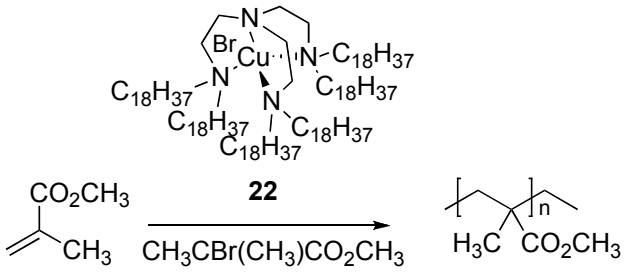
Polyethylene or Oligoethylenes as Supports for Catalysts

About 20 years ago, Bergbreiter's group introduced the use of saturated hydrocarbon oligomers as catalyst supports.[43-45] That work showed that polyethylene (PE) oligomers with a wide variety of terminal ligands could be prepared and could function as thermomorphic supports for recoverable catalysts. These low molecular weight versions of polyethylene are useful because their phase behavior is profoundly affected by temperature. Below about ca. 50 °C, PE oligomers with an M_n of ca. 1200 are completely insoluble in all solvents. Above about 70 or 80 °C they are quite soluble in nonpolar or slightly polar solvents like toluene or dibutyl ether. Such supports can be separated as solids at room temperature by centrifugation or filtration, but during catalysis at elevated temperatures in the appropriate solvents they are soluble and behave like their low molecular weight counterparts.

While most reports where polymeric or oligomeric alkanes have been used as thermomorphic ligands for polymerization catalysts appeared over 10 years ago, this strategy for catalyst recovery/reuse/separation has recently received more attention.[45-47] In 2004, the Vincent group described using multiple octadecyl groups on a CuBr-tren complex to prepare an ATRP catalyst **22** that was both highly reactive and more stable to aerobic conditions. This complex exhibited the same thermomorphic solubility temperature behavior in 1,4-dioxane that had been seen for the larger oligomeric polyethylene oligomers studied by others in other solvents and served as a catalyst in a Cu(I) mediated polymerization of vinyl monomers (e.g. eq. 34). These hexa(C_{18}) tren

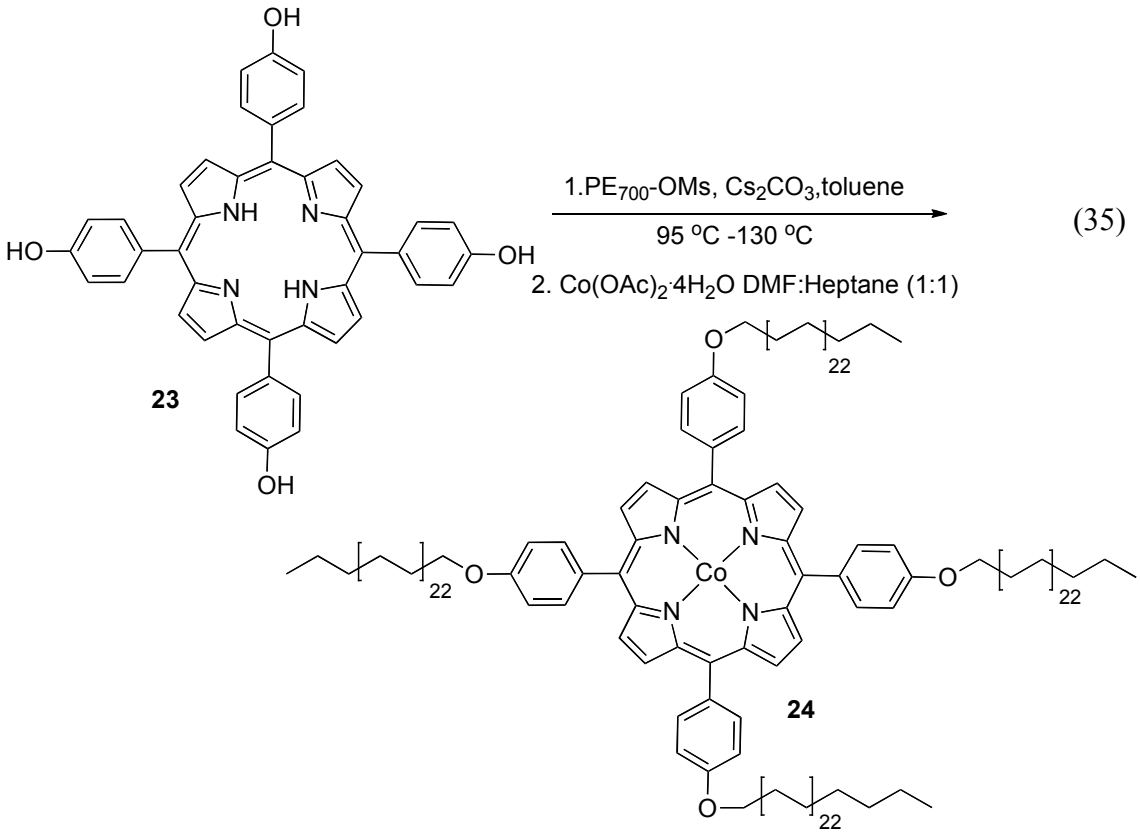


(34)

complexes and were completely recoverable after a polymerization reaction by simply cooling the reaction mixture.[48]

Another recent report on thermomorphic polyethylene supported porphyrins by DuPont suggests that the thermal responsive solubility of these polyethylene oligomers may afford catalysts that are commercially viable thermomorphic catalysts for free radical polymerization or copolymerization of styrene or methacrylates.[49] Such catalysts can be prepared using functional groups on the periphery of porphyrins like **23** using commercially available polyethylene oligomers (eq. 35). The resulting polyethyl-ligated catalysts **24** are not any more reactive than the porphyrin catalysts already used for this industrial process. However, unlike low molecular weight catalysts, the polyethylene-bound catalysts can be completely separated from the desired product. In this case, the polyethylene oligomer-supported porphyrins are soluble under the higher temperature used for the polymerization chemistry but quantitatively precipitate on cooling. They can then be removed by filtration or centrifugation. In the application described, these polyethylene-bound catalysts are used to prepare metal- and color-free polymer products with controlled molecular weights. The macromonomers produced in these processes are ultimately used in coatings (e.g. automotive paints) and these separable catalysts

avoid problems with the color imparted by trace contamination from more conventional catalysts. The idea behind this PE-supported porphyrin by Dupont is in sharp contrast to Bergbreiter's work on polyisobutylene (PIB)-bound Cu(I) complexes for atom transfer radical polymerization (ATRP) of styrene[50], which will be discussed in more details later under 'PIB as a soluble support for ligands and catalysts' section of this dissertation. In the case of PIB-bound Cu(I) complexes, the product polystyrene was able to be isolated via simple filtration as solids due to the self-separating nature of the system.



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Liquid/Liquid Separation of Polymer-Bound Ligands and Catalysts

Liquid/liquid separations are ubiquitous in chemistry. Indeed most organic reactions involve a gravity separation of two phases of different density and polarity in the work-up steps. This same concept of separations also has precedent in homogeneous catalysis for separation of catalysts and products too.[51] Processes like the SHOP process and later processes like the Ruhrchemie/Rhone–Poulenc (RCH/RP) oxo process commercialized in 1980s,[51,52] advantageously immobilize a catalyst in one of the two liquid phases to facilitate catalyst recovery and reuse. More recent biphasic systems that use organic solvents,[53,54] fluorous solvents,[55] ionic liquids[56,57] and supercritical fluids[58] have been developed and used in a variety of catalytic transformations over the past two decades. The use of soluble polymer supports to bind a catalyst and ensure high levels of catalyst and ligand recovery in liquid/liquid separations in biphasic liquid/liquid systems is a more recent concept.

When a liquid/liquid separation is used, the polymeric catalysts are isolated as a solution at the separation stage. As was true for solid/liquid separation strategies that used soluble polymer facilitated catalysis, catalytic reactions prior to the separation process often involve single-phase conditions. However, sometimes reactions are carried out under biphasic conditions. In some of those cases, partial misciblization occurs or the polymeric catalyst's phase selective solubility is different during the catalytic process. In cases where the reaction involves a single solvent, an extraction is used to either remove the polymeric catalyst from the product or to remove the product from the catalyst. With systems containing mixed solvents, a perturbation induced by a

temperature change (a thermomorphic effect),[59], a perturbation induced by addition of a small amount of a chemical perturbant (a latent biphasic system),[60] or a perturbation induced by product formation (self disassembly)[50] can lead to liquid/liquid biphase separation which can be followed by a liquid/liquid separation of the polymer-bound catalyst and product phases. All liquid/liquid separations rely on a gravity based separation of two liquid phases to recover and separate the catalyst. All useful liquid/liquid separations require a soluble polymer-bound catalyst to have high phase selective solubility.

As is true in some solid/liquid separations, liquid/liquid separations of mixed solvent systems can often be carried out without exposing the catalyst mixture to air or water. This can be advantageous if the catalysts or their ligands are air or moisture sensitive because there is no need to open the reactor and transfer the reaction mixture to another container for a workup.

The catalytic process of interest affects the choice of solvents and polymers for liquid/liquid separations. First, solvents suitable for the catalytic process have to be used. Second, if miscible solvents are used, they can be miscible under the reaction conditions but it must be possible to perturb this mixture so that it is biphasic during the separation step. Third, if a thermomorphic, latent biphasic, or self-disassembling separation is used, it has to be experimentally practical to separate the two liquid phases. For example, formation of a biphase with two solvents nearly equal in density will yield an emulsion whose separation will be difficult. Likewise, a liquid/liquid separation that only occurs far from ambient temperature would make a separation less practical.

Fourth, the solvents used have to be acceptable. While equal volumes of Et_3N and water are miscible at 0 °C and immiscible at 25 °C,[61] Et_3N is noxious enough that it is unlikely that such separations would be widely used. Finally, liquid/liquid separations would not be feasible in some cases. For example, while separation of heptane and aqueous ethanol is feasible in general, but it might be impractical if a particular product acted as an emulsifying agent for heptane and aqueous EtOH.

The nature of the polymer support is another consideration if liquid/liquid separations of a polymer-supported catalyst and product are to be effective. For a liquid/liquid separation using soluble polymer supports, to be useful, the polymer-bound catalyst must preferentially dissolve in one of the two phases and products in the other. Thus, polar polymer-bound catalysts are more suitable for preparing nonpolar products and vice versa. A more subtle facet of this issue is that while a soluble polymer and hence the polymer-bound catalyst can have very high (>99.99%) phase selective solubility in one phase of a liquid/liquid biphasic system, low molecular weight products often have some solubility in both phases. Thus, some of the product is often 'lost' to the catalyst-containing phase in the first few cycles of a liquid/liquid based recycling process involving a soluble polymer-bound catalyst. This 'loss' of product can be mitigated by an extraction. It is also arguably less important when a catalyst is recycled numerous times.

Water/Organic Biphasic Systems

Water is generally considered to be the most environmental benign solvent. Many biphasic systems that include water as a solvent immobilize the catalyst in the aqueous

phase.[62-65] Because many organic products are insoluble in water, complete separation of catalysts from products can be achieved easily. However, a biphasic catalytic process can introduce kinetic problems. In some cases, partial solubility of catalyst or substrate in the other phase or efficient mixing can alleviate these problems and reasonable reaction rates can be achieved. This is the case in the Ruhrchemie/Rhone–Poulenc (RCH/RP) oxo process for the production of butyraldehyde from propene where a water soluble triphosphine ligated Rh(I) complex is used to catalyze the hydroformylation of alkenes.[66,67] However, such chemistry is often restricted to a few substrates. For example, in the RCH/RP process other more lipophilic substrates, e.g. larger 1-alkenes, are not readily hydroformylated.

Thermoregulated Phase Transfer Catalysis

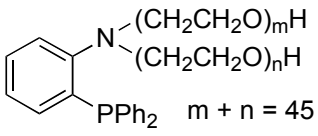
Poly(ethylene glycol)'s history as a soluble polymer support was discussed above. These polyether polymers, like the PNIPAM-supports described above, exhibit LCST (lower critical solution temperature) behavior. However, unlike PNIPAM, poly(alkene oxide)s often separate as an oil above their LCST. This LCST behavior of poly(alkene oxide)s in water has been used to design a process termed "thermoregulated phase-transfer catalysis" (TRPTC) by Jin's group.[68-71] Rhodium catalysts attached to these sorts of polymers have been successfully used in hydroformylation of higher olefins which are not suitable substrates in RCH/RP processes using a biphasic liquid/liquid mixture of water and an organic solvent. In these TRPTC systems, the polymer-bound catalysts' inverse temperature dependent solubility makes them soluble in an aqueous phase at a temperature below their LCST. However, at their LCST the polymer's

solubility changes. Since poly(alkene oxide)s separate as an oil-in-water emulsion at their LCST, these polymers and catalysts bound to them can partition into the organic phase tht is present. In cases where the substrate is present in that organic phase, the reaction does not occur to any appreciable extent below this LCST because the catalyst concentration is low. However, above the LCST, the catalyst concentration in the organic phase increases and reaction occurs. Cooling after the reaction is complete allows the polymer-bound catalyst to partition back into the aqueous phase where it can be recovered.

An example of thermoregulated catalysis is the hydroformylation of 1-decene in a water/toluene system using the PEG-supported *P,N*-bidentate triphenylphosphine ligand **25**.[72] In this case the catalyst was generated *in situ* by reaction of $RhCl_3.3H_2O$ with **25**. Catalytic reactions were carried out using 0.1 mol% Rh catalyst at 120 °C and, under these conditions, essentially 100% conversion of alkene to aldehydes product was seen. A slight disadvantage to this system was a lower *n*:*iso* selectivity in the range of 0.60-0.64 due to the increased alkene isomerization at the 120 °C reaction temperature.

While the level of Rh leaching into product phase was not measured, good recycling efficiency was evident from the fact that after 20 cycles the yield of aldehyde and the TOF number of the catalyst were 94.4% and 189 h^{-1} as compared to 99% and 198 h^{-1} in the first cycle. The high recyclability of the Rh catalyst in the water phase suggests both a high phase selective solubility for the catalyst and good catalyst stability, a stability that the authors attributed to P-N chelation of Rh by the ligand.

These recycling results suggest a high phase selective solubility for Rh complexes of the ligand **25** during the catalyst/product separation step. However, this successful hydroformylation could not be solely attributed to the ligands' LCST behavior. Specifically, the biphasic hydroformylation reaction still occurred below the LCST. When a Rh catalyst was prepared using **25** (LCST = 92 °C), a ca. 40% increase in conversion from ca. 65% conversion to ca. 85% conversion was seen as the biphasic toluene/water mixture of catalyst was heated through the LCST temperature (i.e. from 90 to 100 °C).[72]



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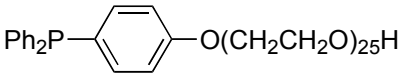

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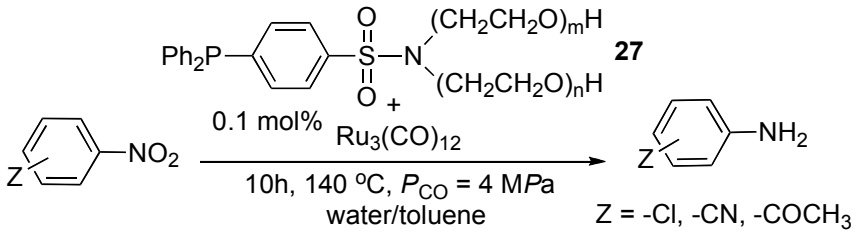
Further studies of hydroformylation using catalysts that have LCST behavior showed that even a very hydrophobic internal alkene, oleyl alcohol, afforded a good (81%) yield of aldehyde products that decreased minimally to 78% through four cycles using a very simple monovalent PEG-phosphine ligand **26**.[73]

A Ru complex of ligand **27** has also been used to reduce nitroarenes to aniline derivatives using CO as the reductant (eq. 36).[74] While no analyses for Ru were reported, only a slight loss of activity over four cycles was observed when recycling these catalysts.



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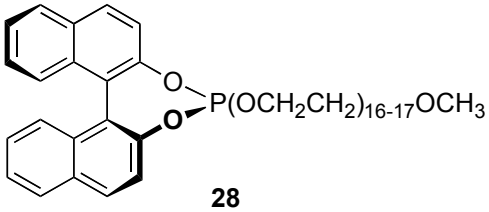
Attempts at enantioselective hydroformylation of styrene under TRPTC conditions have been reported by Breuzard and co-workers.[75] In this work, the catalysts were generated *in sit*u by allowing a PEG-supported chiral phosphite ligand **28** or **29** derived from (*S*)-binaphthol to react with $[Rh(cod)_2BF_4]$ in an aqueous solution. Very modest enantioselectivity, ca. 25% ee, was achieved using ligand **29**. Moreover, recycling was unsuccessful for either polymer-bound ligand. This might be attributed to the use of relatively short PEG chains in the ligand syntheses. Alternatively, there could have been some catalyst decomposition. ^{31}P-NMR spectroscopic studies of recovered catalyst/ligand or ICP analyses for Rh might have addressed this issue but were not reported.



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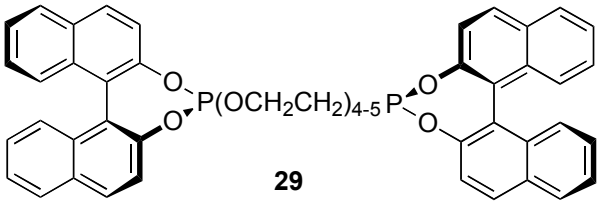


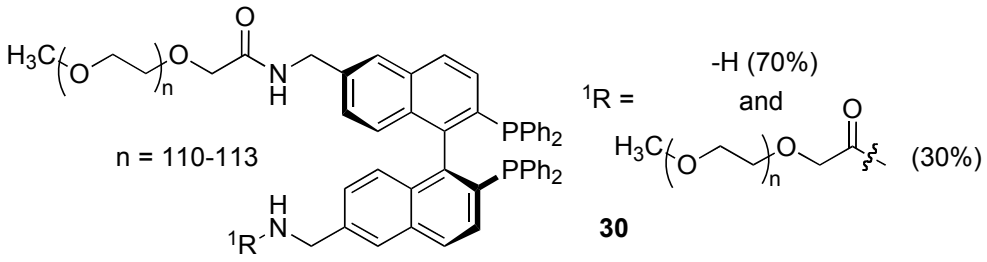
29

Smart catalyst that coupled a catalyst to a soluble responsive polymer were described by our group earlier in our efforts to develop recoverable catalysts.[76,77] More recently, Davies and Stringer found that an aqueous solution of poly(alkene oxide)s (Poloxamers) can serve as a smart reaction medium that exhibits anti- or hyper-Arrhenius behavior.[78] In these cases, the polymer was not used in a catalyst recovery step. Rather the highly temperature dependent critical micelle concentration (cmc) of these polymers was used to design systems where reactions were turned ON or OFF above a particular temperature. For example, an exothermic reaction containing hydrophobic and hydrophilic reactants was turned OFF after all the hydrophobic reactant was transferred into micellar pseudophase formed at higher temperature. It was turned back ON once the reaction mixture was cooled. More interestingly, hyper-Arrhenius behavior with a significantly accelerated reaction rate was seen in cases where the reactants and catalyst both partitioned into the micellar phase.

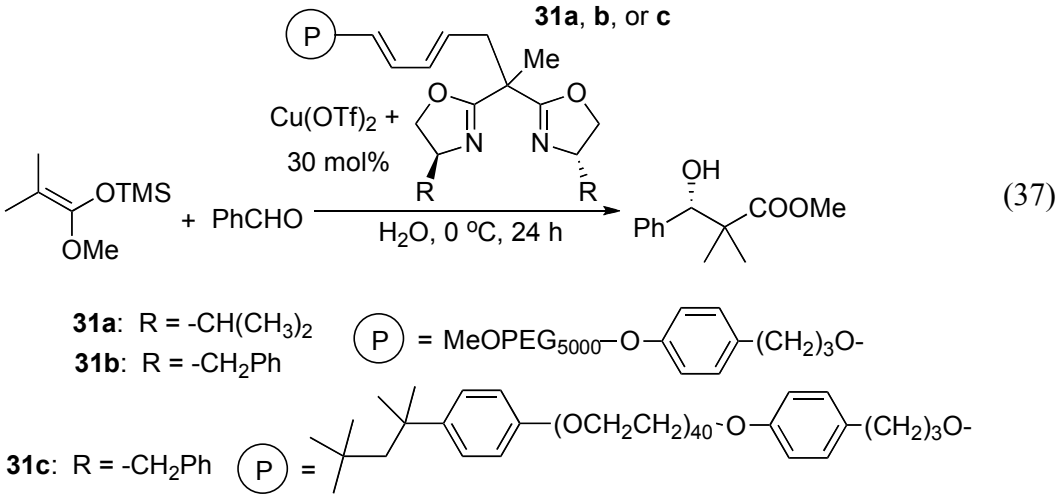
Aqueous Biphasic Catalysts Separable by Extraction

Saluzzo and coworkers reported another PEG-supported BINAP ligand **30** and its use in Ru-catalyzed aqueous biphasic asymmetric hydrogenation of ketones.[79] The PEG-bound Ru catalyst was prepared in DMF by reaction of $[RuCl_2(benzene)]_2$ with **30**. Initial tests of this Ru catalyst under aqueous biphasic conditions were conducted with acetophenone as a substrate in the presence of (*S*,*S*)-diphenylethylene diamine. After a biphasic reaction and pentane extraction of the product, the aqueous phase containing the Ru-catalyst was reused. Recycling was evaluated in the hydrogenation of ethyl acetoacetate to form ethyl 3-hydroxybutanoate. The polymer-bound Ru catalyst could

only be reused twice with a large decrease in conversion (from 100% in cycle 1 to 20% in cycle 2) and enantioselectivity (from 75% ee in cycle 1 to 56% ee in cycle 2).



Another example of an aqueous biphasic system with PEG supports was described by Benaglia and coworkers.[80] In their work, PEG-supported chiral bisoxazoline (Box) ligands **31a-c** were prepared and used in $Cu(OTf)_2$ catalyzed Mukaiyama aldol reactions between the trimethylsilyl ketene acetal of methyl isobutyrate and various aldehydes in



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aqueous media (eq. 37). Cu(II) catalysts ligated by either **31a** or **31b** showed that the reaction of the ketene acetal and benzaldehyde proceeded with the highest

enantioselectivity (55% ee) with ligand **31b,** a result that was comparable to results reported by Kobayashi with unsupported ligands in aqueous media.[81] However, poor water-solubility of the aldehyde electrophiles led to relatively low synthetic yields. The use of ligand **31c** slightly improved the enantioselectivity but did not affect the yield. Higher yields were only seen with more polar aldehydes such as 4-nitrobenzaldehyde perhaps because of solubility. These more reactive aldehydes were used to study catalyst recycling. Catalyst recycling was in this case involved separation of the organic product from the aqueous solution of the catalyst by extraction of aqueous phase with diethyl ether. The resulting aqueous phase containing the catalysts was directly reused in a subsequent reaction cycle. These experiments showed that catalysts that used ligand **31c** could not be recycled (the ligand was partly soluble in diethyl ether). However, recycling $Cu(OTf)_2$ complexed by **31b** was successful with only modest decreases in yield (40%-38%) and enantioselectivity (50% -43% ee) through three cycles.

Organic/Organic Biphasic Systems

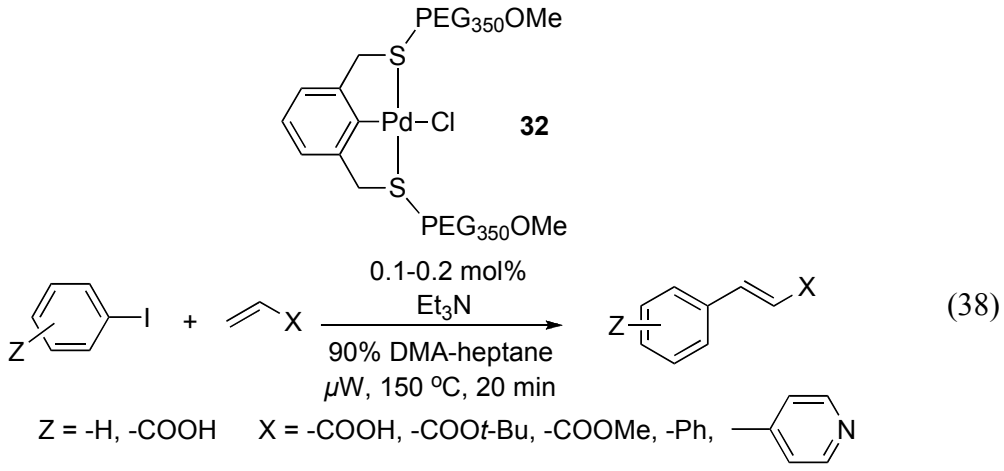
Most organic reactions are still carried out in organic media. Catalysts attached to phase selectively soluble polymer supports can be separated from products, recovered and reused in these systems just as they are in water/organic systems. Three general schemes are used. First, the reaction can be carried out in a mixture of immiscible organic solvents. If the polymer-bound catalyst were phase selectively soluble in a phase different than that favored by the product, the separation would just involve a gravity separation after the reaction. A second and possibly more useful scheme is to carry out a reaction under conditions where the solvent mixture used is a single phase.

Then a phase separation could be triggered by a addition of another solvent, an additive or a temperature change. Gravity separation would then serve to separate and recover the catalyst. Again, a phase selectively soluble polymer-bound catalyst would be required and the product would have to be preferentially soluble in the non-catalyst containing phase. Finally, a reaction can be run homogeneously in a single solvent. Extraction with an immiscible solvent can then remove the product or catalyst if the catalyst was phase selectively soluble in a solvent that was not a good solvent for the product. Phase selective solubility of polymers in one or the other phase of an organic/organic biphasic system is required for any of the above schemes to be viable. Fortunately, polymers often have excellent phase selective solubility – phase selective solubility that is subtly dependent on polymer microstructure.[82,83] Polymers can be molecularly engineered to be soluble only in a polar phase or only in a nonpolar phase. Thus, these organic/organic separation schemes can in principle be implemented in many if not most solvent mixtures.

Thermomorphic Phase Selectively Soluble Polymers

Thermomorphic separations using soluble polymers were first described by our group in 1998 using polar poly(*N*-isopropylacrylamide) (PNIPAM) polymer supports.[59] Subsequent to our initial work with PNIPAM-supported catalysts under thermomorphic conditions, we prepared both PEG and PNIPAM supported SCS-Pd complexes.[84,85] The initial reports of their use in catalysis was discussed in details in the earlier review in 2002 by Bergbrieter.[7] While later studies showed that these complexes are precatalysts and not catalysts for Pd-catalyzed cross-couplings,[86-88] low loadings of Pd complexes

can be used in catalytic reactions to form products with high levels of separation of Pd from the cross-coupling products. For example, the PEG-supported SCS-Pd complex **32** was used in 90% aqueous dimethylacetamide (DMA)/heptane (1:2, vol:vol) in cross-coupling chemistry (eq. 38) under microwave conditions with reactions being complete

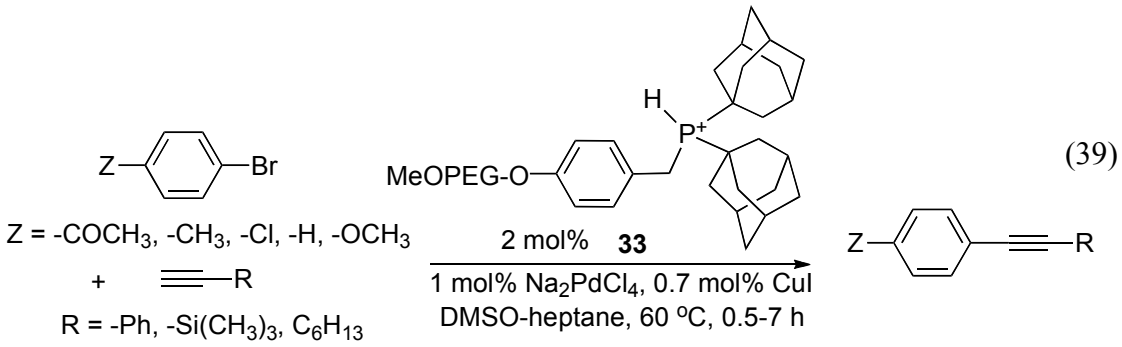


(38)

in 10-30 min with as little as 0.01 mol% catalyst.[89] In this reaction, microwave heating caused the initial thermomorphic biphasic mixture to become miscible. After the reaction, cooling reformed the biphasic mixture. Separation of the polar phase recovered the complex **32** and four recycles were carried out. Pd leaching into the nonpolar heptane phase was measured by ICP-MS and in a reaction using ca. 3 x 10^{-4} M Pd, the amount of Pd lost was < 0.5 % of the charged Pd.

While the polar polymer-bound Pd complex **32** is effective in cross-couplings of aryl iodides and acrylates, the use of less expensive aryl bromides as substrates for C-C coupling reactions is more attractive. Hindered phosphine-ligated Pd catalysts are

efficient in this process[90] because the concentration of more coordinatively unsaturated Pd complexes is larger.[91,92] This aspect of homogeneous Pd chemistry has been extended to thermomorphic polymeric systems using the PEG-supported hindered phosphine **33** to form a Pd catalyst for Sonogashira coupling reactions conducted in a DMSO/heptane (eq. 39).[93] Unreactive aryl bromides were suitable substrates with this more hindered polymer-bound phosphine ligand. This polymer-bound catalyst was successfully recycled through five cycles with overall yields >90%. However, poor recyclability was seen when an aliphatic alkyne was used in place of phenyl acetylene in



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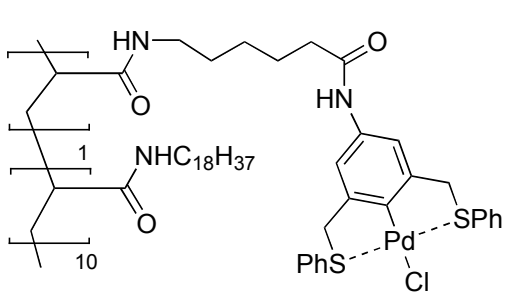
eq. 39. The studies of recyclability of PEG-bound Pd catalyst were more thorough than most such studies. First, the kinetics were examined for three bromoarene substrates – 4-bromoanisole, bromobenzene, 4-bromoacetophenone. The TOF in the first cycles were 336, 440, and 1150 h^{-1} versus a TOF of 252, 312, and 880 h^{-1}in the fifth cycles for these three substrates, respectively. These differences were attributed to in large part to oxidation of the Cu(I) cocatalyst to Cu(II) since the TOF values increased when fresh CuI was added to the reaction mixture. Second, leaching of **33** or Pd into the heptane

phase was negligible based on the absence of the characteristic resonance for the CH_2O-group of PEG on ^{1}H-NMR spectra of the nonpolar phase and analysis by X-ray fluorescence (XRF) for Pd. Based on the sensitivity of the XRF analysis, the retention of both the palladium and copper species in the DMSO phase was estimated to be > 99.995%.

The thermomorphic separations using soluble polymers first described by our group used polar polymers like PEG and PNIPAM. However, polar polymer-bound catalysts in thermomorphic separations have an inherent problem in that both the products and byproducts of most reactions often preferentially accumulate in a polar phase. This affects the conditions necessary for miscibility in a recycling experiment. It also makes catalyst/product separation more problematic. Thus, as our group continued to explore the idea of thermomorphic separations we focused most of our attention on nonpolar polymers for separation of catalysts and products.

An advantage of poly(*N*-alkylacrylamide) supports is their phase selective solubilities are tunable by changing the structure of the alkyl substituents on the nitrogen atom.[82,83] For example, in contrast to PNIPAM, poly(*N*-octadecylacrylamide) (PNODAM) is a lipophilic polymer that has heptane solubility. We prepared PNODAM-supported phosphine and SCS ligands using a procedure like that used earlier to prepare PNIPAM derivatives. Metalation with $Pd(PhCN)_2Cl_2$ and $Pd(dba)_2$ in refluxing THF then led to the Pd complexes **34** and **35** that had high nonpolar phase solubility. The SCS-Pd complex **34** could be used in Heck reactions just like earlier PNIPAM-bound complexes. While the actual catalyst has subsequently been shown to

not be the SCS-Pd complex,[86] reactions using **34** to form cinnamic acid from iodobenzene and acrylic acid could be repeated multiple times without any additional Pd source. For example, after nine cycles conversion was still 90%.[94]



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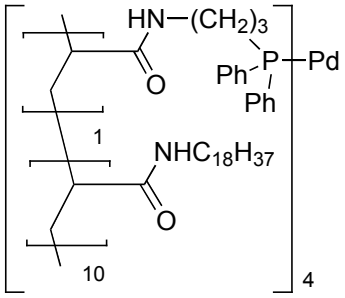

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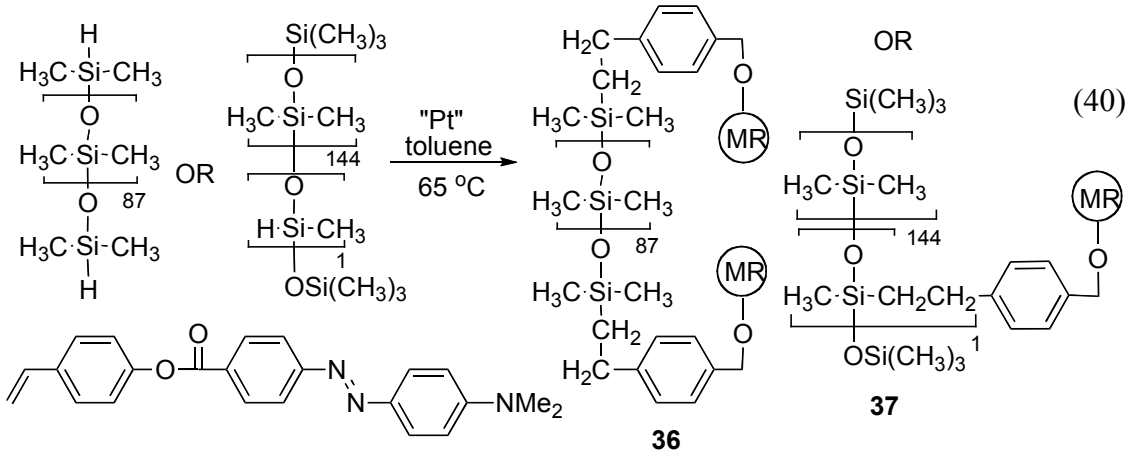
Allylic substitutions that used the Pd(0) catalyst **35** were also reported. While five cycles with this catalyst were successful, gradual deactivation of the catalyst was observed based on the increase in reaction times from 1 h in cycle 1 to 52 h in cycle 5. In this case, the use of a soluble polymer allowed us to examine the catalyst after the reaction. This ^{31}P-NMR spectroscopy analysis showed that oxidation of phosphine ligands during the reaction was the proximate cause of the catalyst deactivation.

Latent Biphasic Separations

The use of temperature as a trigger to induce phase separation of solvents in a mixed solvent system is not always necessary. Product formation or small amounts of additives can have a similar effect and this strategy has been used to advantage with several sorts of soluble polymer-supported catalysts.

Polysiloxanes have been used as supports for the recovery of catalysts but are usually reovered by membrane filtration or solvent precipitation.[95,96] Liquid/liquid phase separations are an alternative to this approach for separation/recovery/reuse of polysiloxane-bound catalysts. The viability of this approach was demonstrated by the synthesis of several dye-labeled polydimethylsiloxanes **36** and **37** (eq. 40).[97] The feasibility of liquid/liquid biphasic separation for both **36** and **37** were studied using either a thermomorphic mixture of heptane and DMF or a latent biphasic mixture of heptane and EtOH. In these experiments, a heptane solution of the dye-labeled polymer was mixed with an equal volume of DMF or EtOH. Heating in the first case generated a monophasic solution that on cooling had 97.6% (**36**) or 99.5% (**37**) of the dye in the heptane phase. In the heptane/EtOH mixture, addition of 20 vol% water produced a biphasic mixture with 99.6% (**36**) or 99.5% (**37**) of the dye in the heptane phase.



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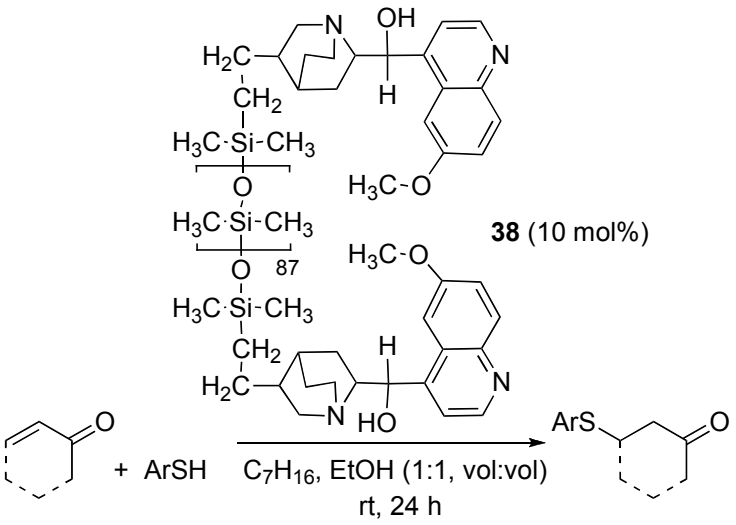
Based on these results, a silane-terminated poly(dimethylsiloxane) was used to hydrosilate a *Cinchona* alkaloid.[97] The product immobilized quinine derivative **38** was then used to catalyze Michael additions of thiophenols to α,β-unsaturated ketones and esters (eq. 41) in a equivolume of EtOH and heptane. Recycling simply involved water addition followed by separation of the catalyst containing heptane phase. This recycled heptane phase containing the polymer-bound quinine **38** afforded 80% to 100% yields of products for each cycle through five cycles. No effort was made to optimize this chiral catalyst and only modest enantioselectivity was observed.



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Polyisobutylene (PIB) as a Soluble Support for Ligands and Catalysts

As noted above, nonpolar polyolefin supports like polyethylene (PE) are readily recyclable. However, their insolubility in polar solvents and their complete insolubility at room temperature in any solvent limited their further use in catalytic processes. More recently, our group has begun to explore polyisobutylene (PIB) as an alternative to these

PE supports. Vinyl terminated PIB is commercially available[98] and its vinyl end groups can easily be modified.[99] An important feature is that the terminally functionalized can be easily analyzed by soluble ^{1}H-NMR spectroscopy as shown in Figure 1. ^{13}C-NMR can be used as well. More usefully, these PIB oligomers are soluble in many nonpolar organic solvents at room temperature. Studies on phase selective solubility using methyl red and dansyl labeled PIB oligomers in a biphasic system consisting of 90% aqueous ethanol and heptane, revealed that these PIB derivatives are selectively soluble in heptane phase of these thermomorphic solvent mixtures to an extent of more than 99.6%.[54,99]

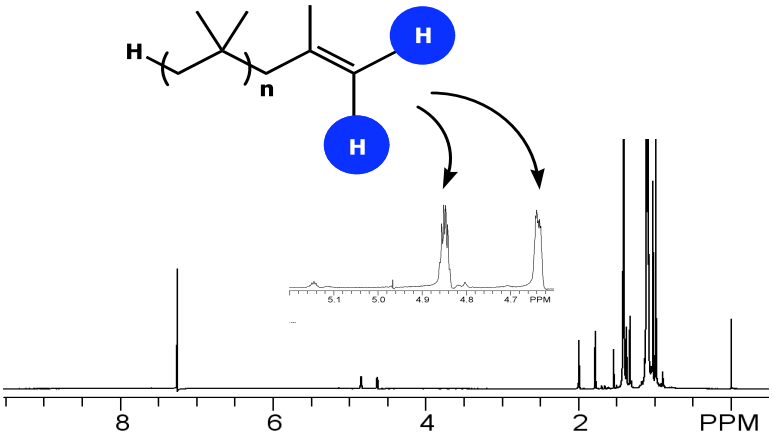
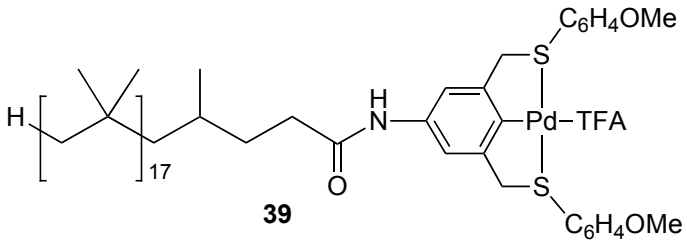


Figure 1. ^{1}H-NMR of vinyl terminated polyisobutylene.

The utility of PIB oligomers as nonpolar soluble supports was first demonstrated in the thermomorphic systems using Pd catalyzed cross-coupling reactions. Both an SCS ligand and a phosphine ligand were attached to the terminus of a PIB oligomer and these



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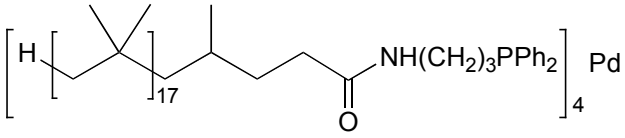

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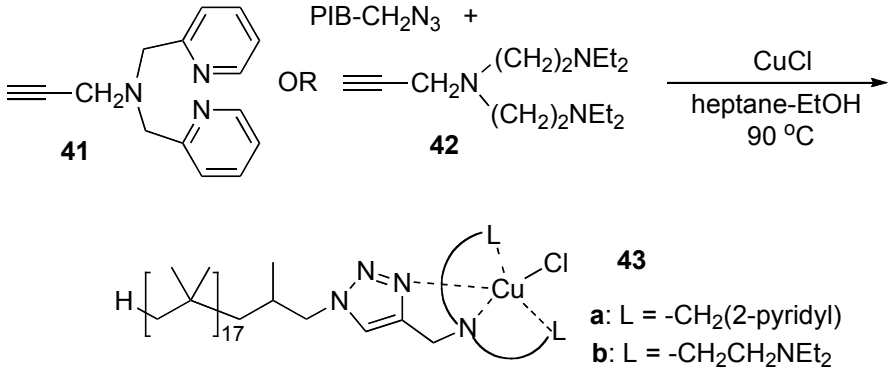
PIB ligands were used to prepare the Pd species **39** and **40**.[88,100] Like other supported SCS-Pd(II) species, the PIB-SCS-Pd precatalyst **39** was only effective for aryl iodides as substrates in Heck chemistry that was carried out at 100 °C. In these cases, an equivolume mixture of heptane and DMA was used as solvent. This solvent mixture was miscible under the reaction conditions but immiscible at room temperature and the Pd in the heptane phase was separated and reused for three cycles without observable loss of activity. Similar results were achieved in a Sonogashira reaction conducted at 70 °C in a monophasic 90% aqueous ethanol and heptane mixture using the Pd catalyst **40** formed from a PIB-bound phosphine and $Pd_2(dba)_3$.

The other example of PIB as nonpolar soluble polymer supports was the report from our group in 2007, where a PIB-bound Cu(I) complexes in ATRP polymerization of styrene.[50] In this report, the properties of the PIB polymer facilitate catalyst separation in two ways. First, the PIB-bound triazole catalyst was prepared in a mixture of heptane and EtOH from an azide-terminated PIB and an alkyne containing a chelating group for

copper (**41** or **42**) using Cu catalysis (eq. 42).[101] After this copper assisted alkyne azide cyclization was complete, cooling produced a biphasic mixture and the polymer-bound



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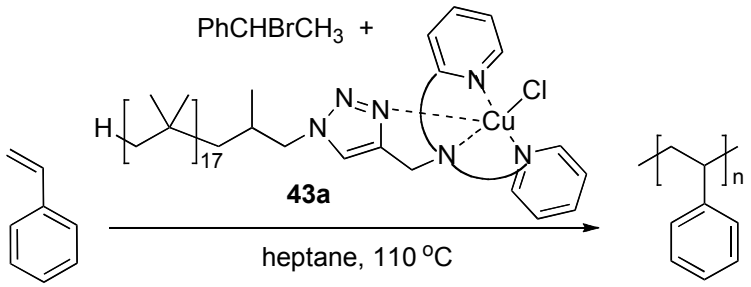
chelated copper complex **43a** or **43b**. This copper complex was isolated as a heptane solution and the heptane solution of **43a** was then used directly in an ATRP polymerization of styrene. This polymerization was carried out using equivolume mixture of heptane and styrene with 1-bromo-1-phenylethane serving as an initiator (eq. 43).



(43)

In this second polymerization step of this catalytic cascade process the miscibility of this heptane/styrene solvent mixture changed as polystyrene formed because polystyrene

is insoluble in heptane. Thus, when a polymerization like eq. 43 was carried out at 110 °C to ca. 50% conversion and cooled, two phases formed with the Cu catalyst **43a** being in the upper heptane phase and the colorless polystyrene being in the lower phase. Using this approach, catalyst **43a** was successfully recycled five times in a styrene polymerization. An average of 50% conversion achieved for each cycle with only ca. 3% of copper loss in the product was detected by ICP-MS. These results suggest that these copper catalysts and this approach should be useful in the synthesis and modification of other sorts of polymers if contamination of products by catalyst residue is of concern.

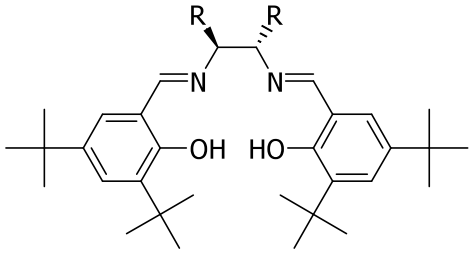
Many of the soluble polymer supported catalysts developed in our laboratory in recent years have used PIB oligomers as nonpolar soluble polymer supports to simplify catalyst recycling and recovery. The progress of our research depends on developing and understanding the phase selective solubility and new synthetic pathways of PIB-supported ligands and catalysts. Processes involving PIB are further described in subsequent chapters of this dissertation.

CHAPTER II

POLYISOBUTYLENE-SUPPORTED SALEN Cr(III) COMPLEX

Introduction

The world "salen" is an acronym widely used to denote a family of bisimine compounds having a structure derived from *N,N'*-bis(salicylidine)ethylenediamine.[102] The imine functional group is generally known as a Schiff base. Salen ligand (**44**) is a very versatile chiral ligand. Many of salen derivatives can be used as ligands to create effective asymmetric environments for many mechanistically unrelated reactions. Such ligands are called "privileged ligands". This term was used by Jacobsen to describe these ligands in the same manner that scientists doing pharmaceutical research have described the broad utility of certain classes of compounds against many different biological targets.[103] Salen ligands bind to metal ions through four atoms. Once the salen-metal complex is formed, the stability of the Schiff base group will increase drastically due to the coordination with metal ion. As a result, salen-metal complexes can be used in wet solvents without undergoing hydrolysis. This tetradentate ligand (**44**) is very similar to the porphyrin framework in heme-based oxidative enzymes. In fact, the oxo-transfer mechanism of heme-containing enzymes such as cytochrome P-450 was the inspiration for the development of chiral manganese-salen complex by Jacobsen and Katsuki who independently co-discovered salen ligands that are used for the asymmetric epoxidation of unfunctionalized olefins.[104,105]



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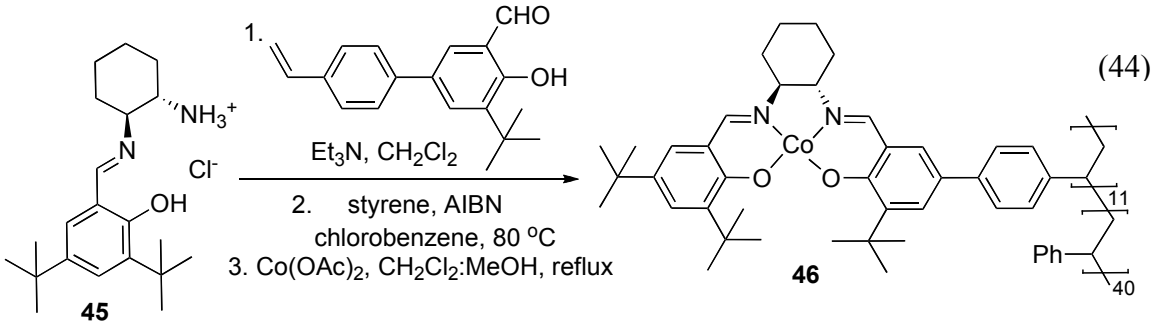
After the initial breakthrough in the use of chiral manganese-salen catalysts for asymmetric synthesis of epoxides, Jacobsen, Katsuki, and other groups expanded the scope of enantioselective catalysis with salens to include other reactions. Their research showed that transition metal complexes derived from chiral salen are among the most powerful enantioselective catalysts. These salen complexes can include transition metals like Mn, Cr, Co, V, Cu, Ti, Ru, Pd, Au, Zn, and Al.[102] Such catalysts afford high enantioselectivity in a wide variety of reactions including alkene epoxidation, epoxides ring opening, cyclopropanations, aziridination, selective hydrogenations, carbonyl cyanosilylation, and imine additions.[102,106] Advantage of salen ligands include their easier synthesis vis-à-vis porphyrins catalysts, and the ability to easily manipulate their structures to create tuned chiral environments around the metal active site through variation of the structure of the diamine. When chiral salen moieties are modified with bulky substituents, a very stereogenic environment at the active metal center is produced which affords the opportunity to effect remarkable discrimination between the two different enantiomers of a product in asymmetric synthesis.[102]

Because salen catalysts are very useful, a number of reports have appeared that discuss ways to use homogeneous and heterogeneous supported salen ligands. These

approaches can be grouped into five categories: noncovalent immobilizations in zeolites, clays, or siloxane membranes, grafting onto inorganic supports such as silica gel, copolymerization of a functionalized salen monomer into an organic polymer, soluble polymeric salen complexes and attachment or build-up of a salen structure onto a preformed polymer. The main focus of this dissertation is on the use of homogeneous polymer supports. Thus, only some of the recent examples soluble polymer supported salen ligands will be discussed below.

Weck's group recently described the use of non-cross-linked polystyrene (NCPS) as a support for salen-Co complexes. In their work, the NCPS-bound salen Co was synthesized by free radical copolymerization of an unsymmetrical styrene-containing half salen monomer **45** with styrene to form an NCPS-bound salen Co catalyst **46** that was then used in hydrolytic kinetic resolutions of epoxides (eq. 44 and 45).[107] After copolymerization, the NCPS-bound chiral salen was metallated with $Co(OAc)_2$ to form a salen Co(II)



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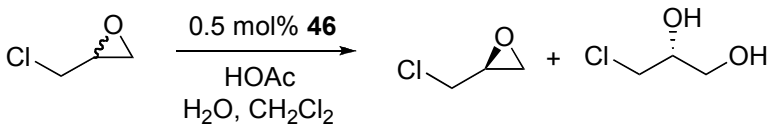
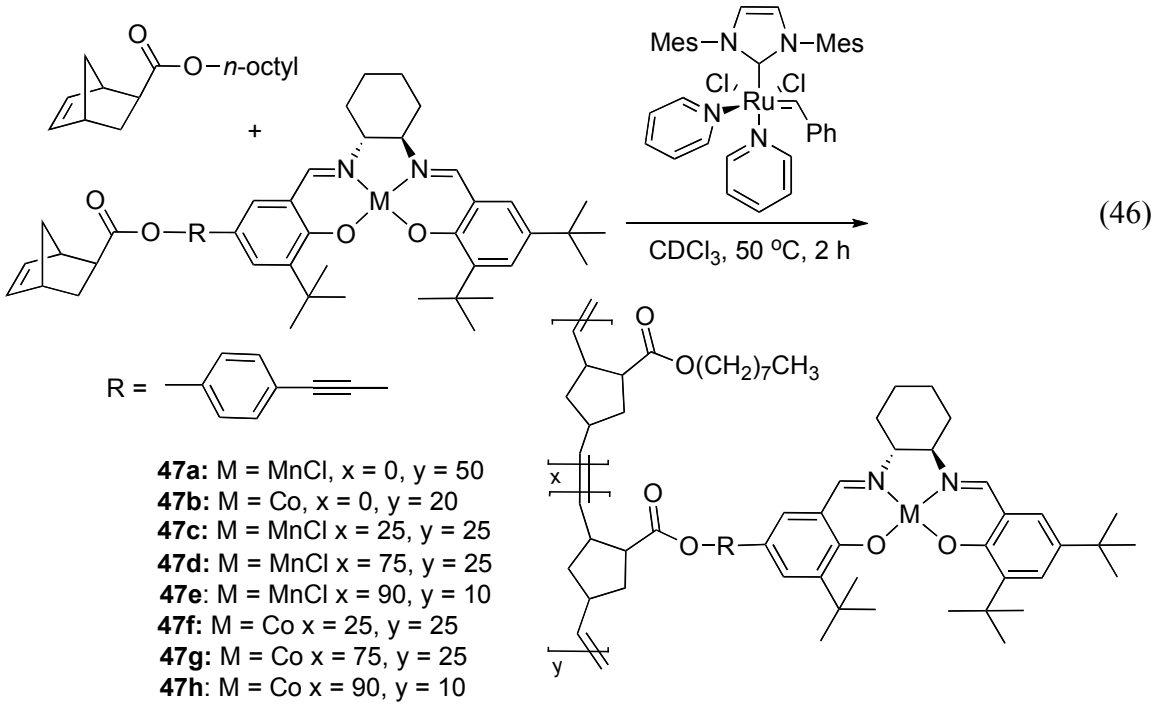


(45)

complex. The resulting NCPS-bound chiral salen Co(II) was oxidized to Co(III) and then used in hydrolytic kinetic resolution of racemic epichlorohydrin. This kinetic resolution (eq. 45) afforded starting material with >99% ee after the ring-opening reaction had proceeded to 54% conversion (1 h). Recycling of catalyst in three successive runs was successful but the reaction time in successive runs was longer reportedly because of physical loss of catalyst during the diethyl ether precipitation/filtration process.

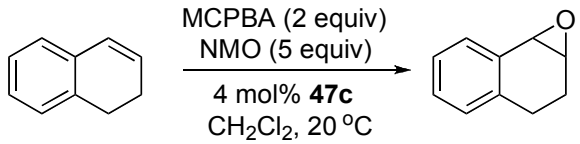
In collaboration with Holbach, Weck expanded his research to include the use of ring-opening metathesis polymerization (ROMP) chemistry with a 3rd generation Grubbs catalyst as a route to polynorbornene-supported salen catalysts where the concentration



(46)

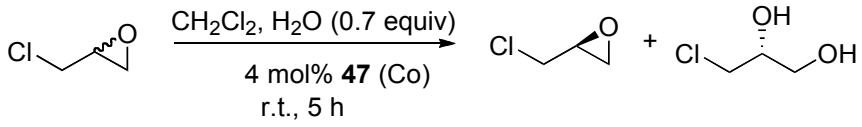
density of the metal salen complex in the polymer was controlled by the presence or absence of a comonomer (eq. 46).[108] Co(II) or Mn(III) complexes of a salen-bound to norbornene via an arylacetylene ester were found to be compatible with the ROMP chemistry. The comonomer was an octyl ester of the same norbornenyl acidused to bind the salen complex. Typical polymer degrees of polymerization (DP) were 50 or 100. Homopolymers of the Co-salen and the Mn-salen complex (DPs of 20 and 50, respectively) were also prepared.

The polymer supported Mn-salen complexes **47a** and **47c-e** were used in the epoxidation of aromatic olefins. For example, the salen-containing copolymer **47c** at 4 mol% catalyst loading quantitatively oxidized 1,2-dihydronaphthalene forming the epoxide with an enantioselectivity of 81%. The results obtained using **47c** as a catalyst were almost the same as those obtained when a low molecular weight salen-Mn(III) complex was used (88% ee). Recycling was examined in this reaction (eq. 47). To recycle and recover the catalyst, the polynorbornene-supported **47c** was precipitated by adding the reaction mixture to a mixture of diethyl ether and methanol. However, while **47c** was recovered quantitatively, **47c** lost its activity and selectivity in recycling in that the conversions dropped to 85% and the product ee dropped to 6% in the third cycle from values of 100% conversion and 81% ee in the first cycle.



(47)

To examine these catalysts in hydrolytic kinetic resolution, the polynorbornene-supported salen Co(II) complexes **47b**, **47f**, and **47g** were oxidized to form Co(III) complexes using acetic acid and air. The Co(III) acetate salen complexes so formed selectively converted the *R* enantiomer of epichlorohydrin to the diol. At 55% conversion, the unreacted *S* epichlorohydrin had an ee of 99%, a result that was very similar to seen with the low molecular weight Co acetate salen catalyst (99% ee at 53% conversion).[109] Kinetic studies showed that the homopolymer catalyst derived from **47b** was slightly less reactive than a structurally similar low molecular weight catalyst under solvent free conditions. However, by oxidizing the Co(II) salen **47b** with O_2 in the presence of *p*-$CH_3C_6H_4SO_3H$, it was possible to prepare a polymeric Co(III) tosylate that was more reactive albeit slightly less selective.

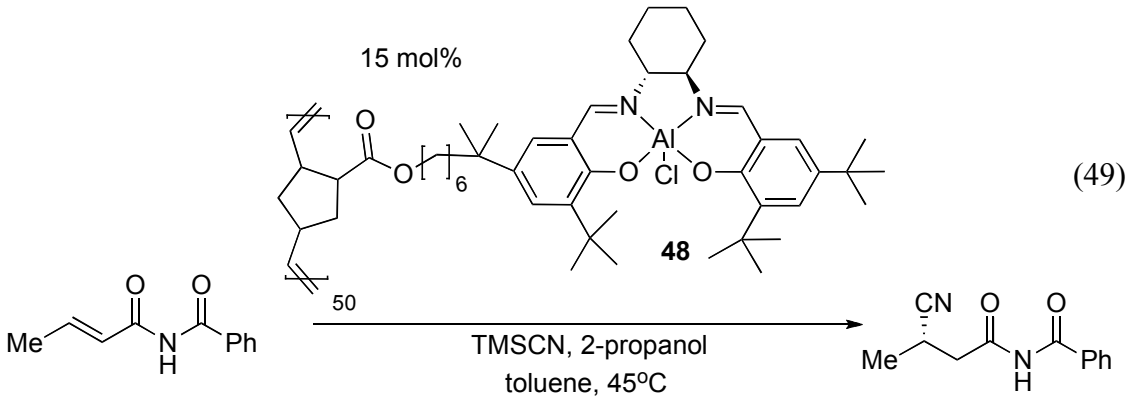


(48)

Recycling of the polymeric Co complexes was possible using solvent precipitation by adding the reaction mixture to excess diethyl ether. The (*R*)-3-chloro-1,2-propandiol product was removed from this ether solution by extraction with water leaving the pure S chlorohydrins. However, the solubility of the recovered Co(III) acetate salen derived from **47b** significantly decreased cycle to cycle and longer reaction times were required for the HKR of epichlorohydrin. Similar studies using a Co(III) tosylate salen derived from polymer **47b** showed that some degradation of the Co(III) salen polymer occurred

based on the changes in the elemental composition of the recovered polymer. The solubility problems encountered with solvent precipitation could be avoided by using an alternative recycling strategy where the substrates were removed by fractional distillation and the catalyst-containing residue was reoxidized in acetic acid with oxygen. Using this method, the reaction time required to obtain the *S* epichlorohydrin in 99% ee increased to ca. 11 h but the aforementioned solubility problems were avoided.

The success of polynorbornene-supported salen Co(II) **47** led to the development of polynorbornene polymers with pendant salen Al(III) complexes (**48**). The salen complex **48** has also been shown to be a useful catalyst for asymmetric conjugate addition of CN to α,β-unsaturated imides (eq. 49).[110] In these reaction the polymer was quantitatively recovered and reused five times without affecting the yield or ee of the product, both of which were >90% so long as the α,β-unsaturated imides did not have a sterically cumbersome group at the β position.



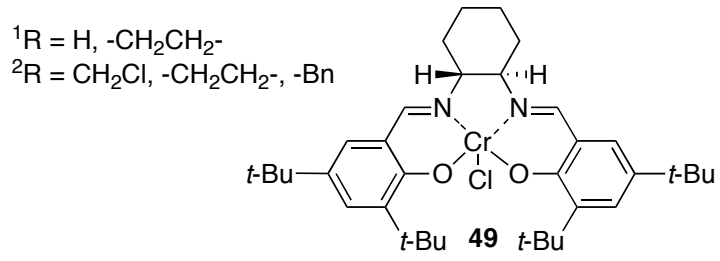
(49)

The recycling procedures used in this example are effective and the catalyst is robust. However, this report also illustrates two of the potential disadvantages of polymer-supported catalysts in general and solvent precipitation in particular as a catalyst recovery procedure. In this report, the examples where catalysts were recycled used 15 mol% catalyst (the authors did note that 5 mol% catalyst was equally effective). These reactions use a mass of catalyst that is nearly equal to the mass of the substrate even though the polymer **48** has a pendant Al-salen group on every repeating unit of the polymer. This level of mass loading is an issue that is not often discussed with soluble or insoluble supported catalysts but is likely a concern if a reaction were to be run on a larger scale and is even more of a problem when the catalyst concentration on a polymer is diluted because it is present as a terminal group or present on a copolymer where its concentration is diluted with another monomer. Second, the workup procedure requires significant solvent to effect catalyst/product separation. In the workup described, the 160 μL of the reaction solvents toluene and isopropanol and the four-fold excess of the toxic trimethylcyanide reagent is removed by evaporation. Then 15 mL of ethyl acetate (EtOAc) was added to the residue to selectively dissolve the reaction products but not the polymeric catalyst. This process is repeated with 4 more 15-mL rinses of EtOAc. Overall this corresponds to the use of 75 mL of solvent for a 0.26 mmol scale reaction. Finally, these recycling studies involved 36 h reactions. Since separate studies showed that the reactions with 15 mol% catalyst were complete in 6 h, these longer reaction times too make it impossible to rule out some catalyst deactivation.

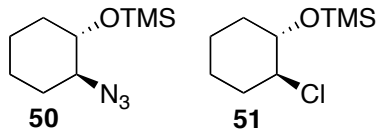
PIB-bound Salen Cr(III) Complex for Ring Opening of Epoxides

The asymmetric nucleophilic ring opening of epoxides is a powerful tool for establishing two stereogenic centers in a single event. The chiral products from the asymmetric ring opening of epoxides such as diols or amino alcohols can be immediately utilized as chiral building blocks for wide ranges of natural products. One of the pioneers in this field is Eric N. Jacobsen. In 1995, Jacobsen's group introduced the use of chiral salen catalysts in the desymmetrization of meso epoxides.[111] Chiral salen catalysts were chosen for their study because of their remarkable success in the asymmetric epoxidation of simple olefins as mentioned earlier in this chapter. Jacobsen believed that the elements of stereochemical communication between substrates and ligands in olefin epoxidation might also apply to epoxides activation by salen metal complex.[111] Jacobsen discovered that the salen Cr(III) complex **49** catalyzes the addition of $TMSN_3$ to meso epoxides with high enantioselectivity (83-98% ee) as shown in eq. 50. The reaction in eq. 50 was carried out neat with epoxides as solvents and the product

(50)

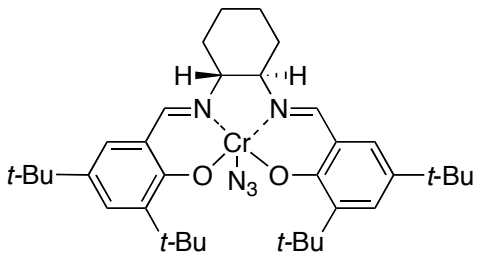


was isolated by distillation. The salen chromium complex **49** could also be recycled four times by addition of fresh epoxides and $TMSN_3$ without the loss in both selectivity and reactivity. However, Jacobsen discovered that during the first cycle, approximately 2%



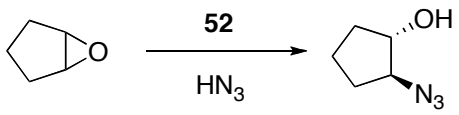
50 **51**

of byproducts (**50** and **51**) formed. These byproducts were not formed during the subsequent cycles. The elemental analysis of catalyst **49** after the first cycle revealed that the nitrogen:chromium ratio of 5:1 and that no chlorine was present. This discovery led Jacobsen to hypothesize that the salen Cr(III) complex **49** was only a precatalyst with the Salen Cr-N_3 complex **52** formed *in situ* being the actual catalyst. The strong IR absorbance at 2058 cm^{-1} was consistent with a Cr-N_3 stretch, which supported Jacobsen's hypothesis. However at this point whether enantioselective epoxide ring opening involved Lewis acid activation by chromium center or nucleophilic delivery of azide by a salen Cr-N_3 intermediate was not established.



52

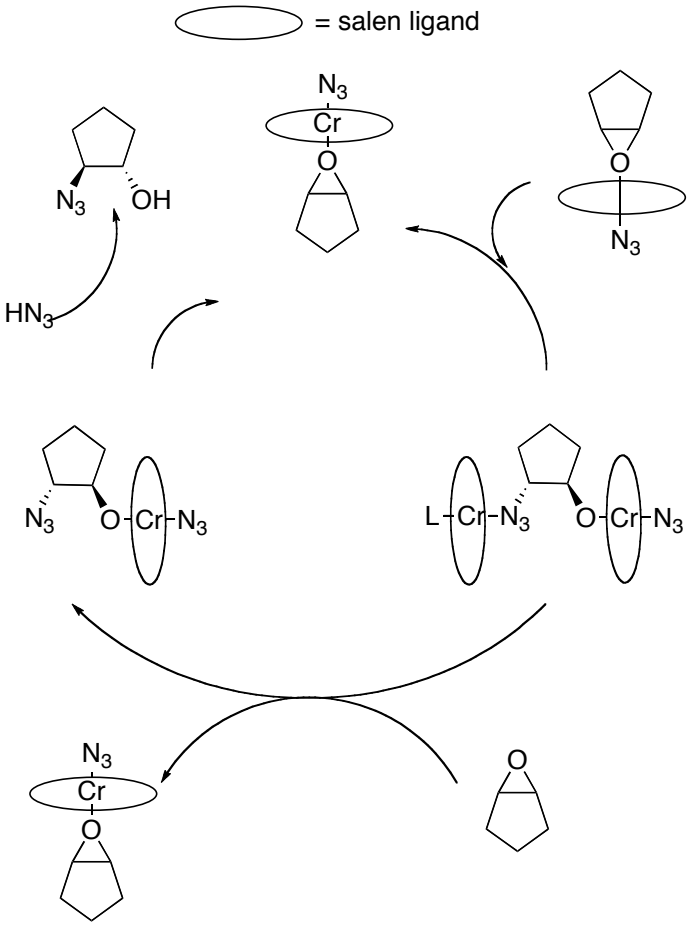
In 1996, a mechanistic study by Jacobsen's group revealed that both processes were involved in asymmetric nucleophilic ring opening of epoxides.[112] Jacobsen conducted the study using only salen Cr(III) complex **52** as a catalyst and HN_3 as a nucleophile as shown in eq. 51. The kinetic runs performed on the catalytic reaction of HN_3 with a greater than five fold excess of epoxides in the presence of **52** were reproducible and revealed a zero-order dependence on the concentration of HN_3. However the rate constant (k_{obs}) was linearly correlated to the square of the concentration of **52** indicating that the reaction was second-order in catalyst concentration.



(51)

These kinetic data provide strong supports for a mechanism involving catalytic activation of both the nucleophile and the electrophile in bimetallic rate-determining steps as shown in Scheme 2. This study provided a critical insight into the catalytic mechanism for salen Cr(III) catalyzed ring opening of epoxides. On the basis of these results, Jacobsen's group sought to improve on salen ligands by exploring the application of the bimetallic catalysts that made of salen ligands capable of simultaneously activating both the electrophile and the nucleophile in enantioselective reactions.

Scheme 2. Bimetallic mechanisms of salen Cr(III) catalyzed asymmetric nucleophilic ring opening of epoxides.



As mentioned above, Jacobsen's group sought to use the existence of the bimetallic pathway mechanistic role of salen Cr(III) complexes to improve upon the previous generation of salen metal complexes **52**. This cooperative bimetallic pathway uses two salen Cr(III) complexes with one complex acting as a Lewis acid that activates the epoxides substrate with the other acting as a nucleophilic delivery agent. Based on this analysis, Jacobsen synthesized a covalently linked dimeric salen Cr(III) complex (**53**).[113]

The principle goal in the design of dimeric analogues of **52** was to convert the intermolecular bimetallic process into the intramolecular process as shown in Figure 2.

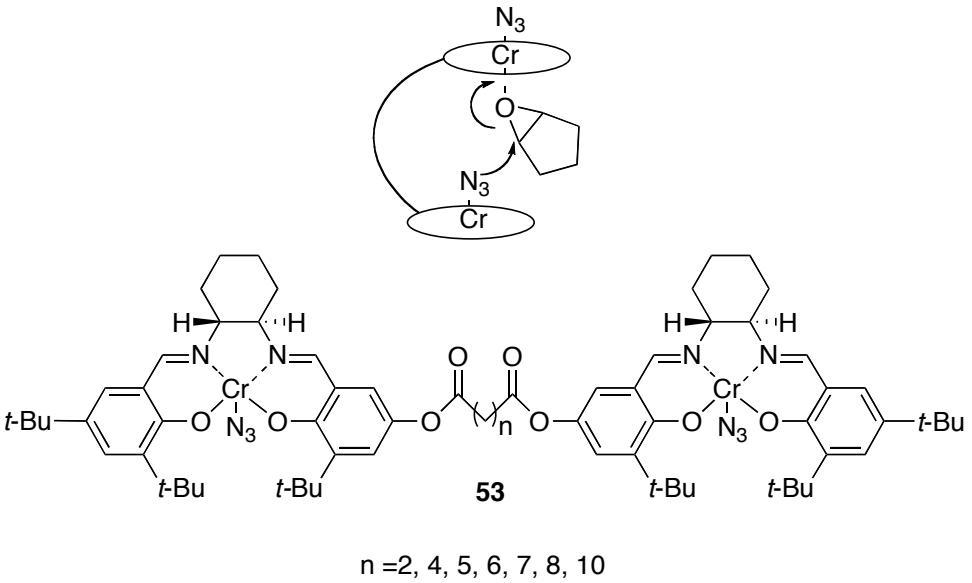


Figure 2. Proposed mechanism of cooperative bimetallic asymmetric ring opening of cyclopentene oxide catalyzed by **53**.

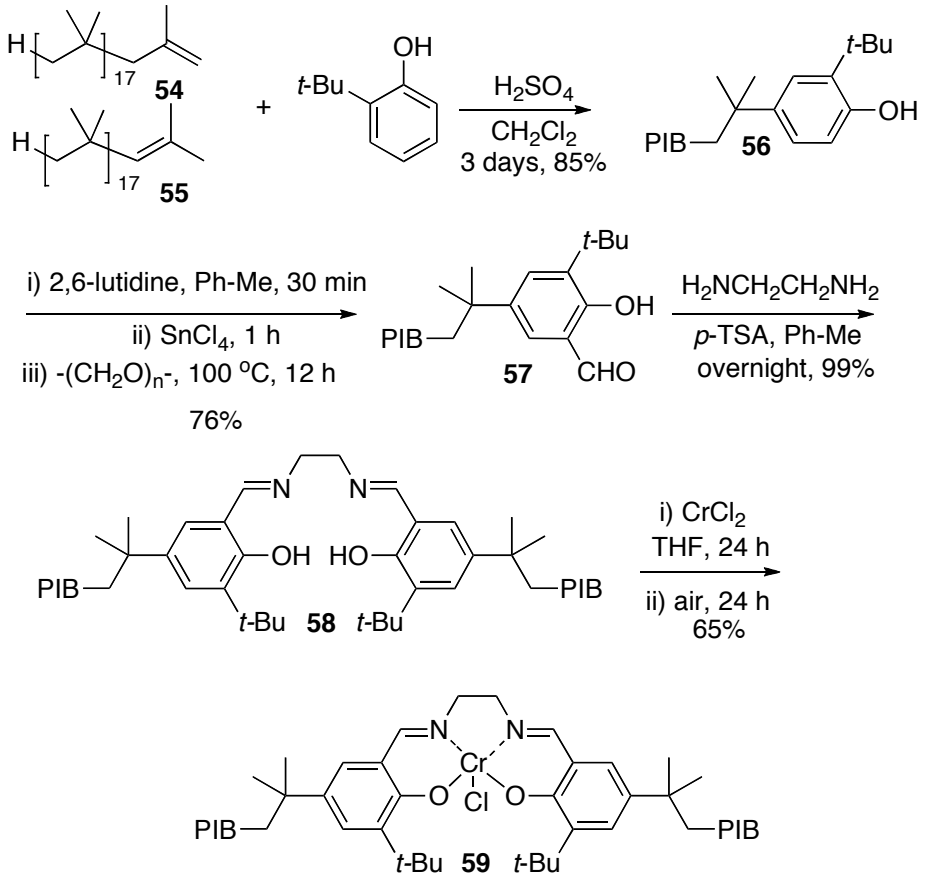
The results of this work showed that the covalently linking Salen Cr(III) units of the asymmetric ring opening catalysts together provided a 1-2 order of magnitude improvement in reactivity over that of their monomeric catalysts. This increase in reactivity was achieved without a loss in enantioselectivity. The success of these dimeric salen Cr(III) complexes also reinforced the initial finding of the bimetallic activation mechanism catalyst **52**.

Thus far salen metal complexes have proven to be very interesting, capable, and versatile catalysts for asymmetric catalytic epoxide ring opening processes reactions that

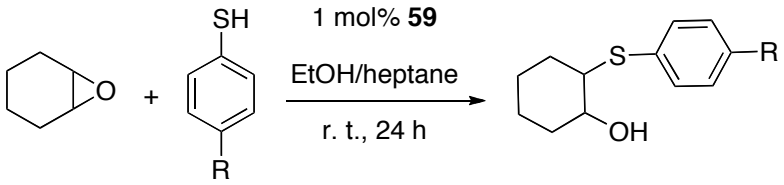
proceed with a unique bimetallic activation mechanism. Since these initial studies, many different groups have studied attachment of salen metal complexes to both soluble and insoluble polymer supports.[102] Some of these soluble polymer supports salen were discussed earlier in this chapter as examples. Other approaches though merit attention because of the importance of recovery, recycling, and separation issues involving salen catalysts. This led us to study PIB supports as discussed below.

Our synthesis of a PIB-supported salen Cr(III) complex started with commercially available vinyl-terminated polyisobutylene. This material is mostly vinyl terminated (i.e. it can be >90% $=CH_2$ terminated **54**). However all samples contain some of the structurally isomeric polyisobutylene oligomer that contains an internal double bond (e.g. **55**). However, both isomers yield the same 4-(polyisobutyl)-*tert*-butylphenol product **56** in an H_2SO_4-catalyzed Friedel-Crafts reaction with the activated arene 2-*tert*-butylphenol in dichloromethane. Further treatment of this oligomeric phenol using paraformaldehyde alkylates and then oxidizes the intermedi-ate benzyl alcohol to in turn produce the 3-*tert*-butyl-2-hydroxy-5-(polyisobutyl)benzaldehyde **57**. This product directly leads to the polyisobutylene supported salen ligand **58**. The ligand **58** was then metallated using $CrCl_2$ and oxidized to form the desired polyisobutylene salen Cr(III) complex **59** (Scheme 3).

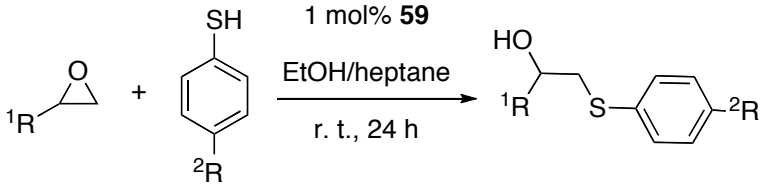
Scheme 3. Synthesis of polyisobutylene supported salen Cr(III) complex **59**.



The PIB-bound Salen Cr(III) complex so formed was then studied as a catalyst for epoxide ring opening reactions. It first was used to catalyze ring opening of epoxides with thiols as shown in eq. 52-53.[114] A latent biphasic system composed of heptane and EtOH was chosen because PIB is 99.6% selectively soluble in the nonpolar heptane-phase versus the polar 90% EtOH/water-phase. We specifically examined three different sets of epoxides and aromatic thiols. The products were isolated without further purification and identified by ^{1}H and ^{13}C-NMR spectroscopy. The results are

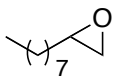
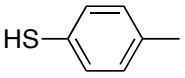
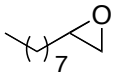
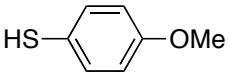
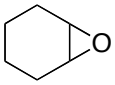
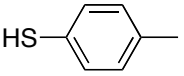
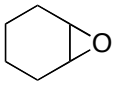
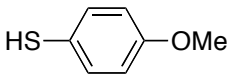
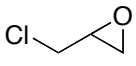
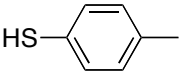
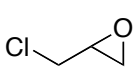
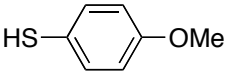


(52)



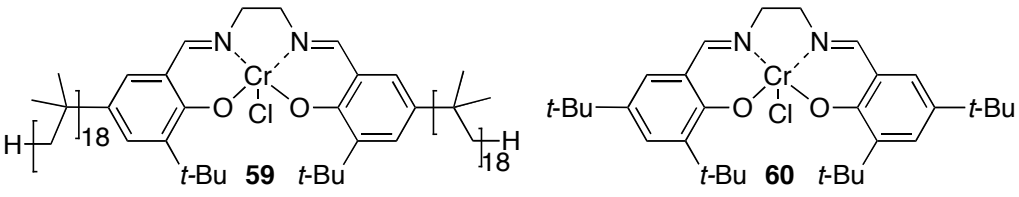
(53)

Table 1. Ring opening of epoxides with thiols catalyzed by PIB-supported salen Cr(III) **59**.

epoxides	thiols	cycle 1	cycle 2	cycle 3	cycle 4	cycle 5
		77%	76%	99%	99%	
		34%	42%	81%	93%	99%
		76%	84%	84%	95%	96%
		94%	90%	99%	99%	
		58%	55%	88%	78%	99%
		73%	70%	84%	98%	99%

shown in Table 1. The recycling process simply involved adding fresh substrates solution in 100% ethanol to the recovered heptane phase that contained the salen catalyst. The catalyst could be used through at least 4 cycles without a loss in reactivity. Inductively coupled plasma mass spectrometry (ICP-MS) analysis of the product containing polar-phase showed only 0.26% chromium leaching per cycle.

The kinetic runs were performed on the ring opening of glycidol with thiol using **59**. A plot of the natural log of [glycidol] vs. time (Figure 3) for low PIB-bound salen Cr(III) compared to similar data obtain using the low molecular weight analog **60** in Figure 3. The result shows that the rate of reaction on the PIB-bound salen complex **59** is virtually identical to that of its low molecular weight analog. The kinetic plot of the second cycle of **59** also revealed changes in the rate of reaction in the second cycle, when compared to the first cycle. This finding was in agreement of Jacobsen's earlier findings in his investigation of ring opening of epoxides with $TMSN_3$, which indicated that the salen Cr-Cl was the precatalyst and the salen Cr-nucleophile is the actual catalyst.[111] The second and third cycle had virtually identicle rates, therefore indicated that **59** did not lose reactivity in the subsequent cycles.



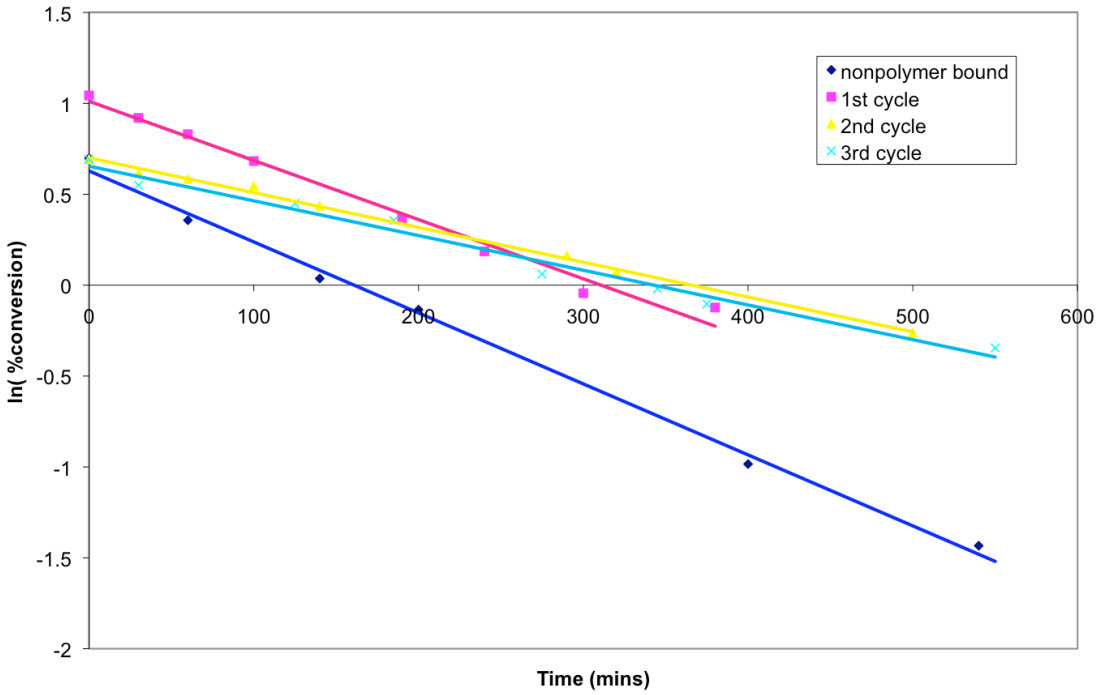


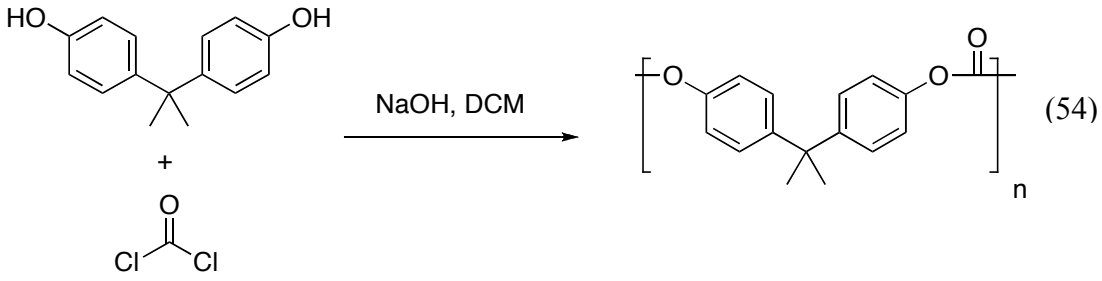
Figure 3. Rate of ring opening of epoxides catalyzed by **60** vs. the first three cycles catalyzed by PIB-bound salen Cr(III) **59**.

Thus far, we have described the synthesis and evaluation of polyisobutylene oligomers as a soluble polymer support for salen Cr(III) complexes that usefully catalyze symmetric epoxide ring opening reactions. These studies showed that the activity of the PIB-bound salen complex is analogous to that of the non PIB-bound Salen complex. Since these nonpolar oligomers were attached to the salen ligand through an unreactive C-C bonds that were distal to the metal center and since the chemistry required involved with a simple synthesis that did not required the use of column chromatography, we thought this chemistry should thus be useful for a wide range of salen ligands where the nonpolar character of polyisobutylene could insure that a salen catalyst was easily

recoverable in the nonpolar phase by a liquid/liquid separation. We expect, for example, that these studies can be extended in the future by using PIB as a support for chiral salen ligands.

PIB-bound Salen Cr(III) Complex for Polycarbonate Polymerization*

Polycarbonates are engineering polymers with outstanding properties that include high tensile strength, lightness, durability, high transparency, heat resistance, and useful electrical insulating ability.[115] However, the classical yet hazardous and expensive production process for synthesis of these polymers shown in eq. 54 that involves the polycondensation of phosgene and diols such as bisphenol A (BPA) is a textbook example of chemistry fraught with environmental problems.[116] In 1969, a greener route



(54)

to high molecular weight po lycarbonates from carbon dioxide and epoxides was reported by Inoue and coworkers using heterogeneous zinc catalysts derived from

* Reprinted with permission from "A phase separable polycarbonate polymerization catalyst" by Hongfa, C.; Tian, J.; Andreatta, J.; Darensbourg, D. J.; Bergbreiter, D. E. *Chem. Commun.* **2008**, 975-977, Copyright 2008 by the Royal Society of Chemistry.

diethylzinc and water.[117] This discovery subsequently led to work in 2000 by Jacobsen and coworkers who patented the use of the (*R,R*)-enantiomer of salen Cr(III) complex **52** as a catalyst in a selective reaction of one atmosphere CO_2 with the (*S*)-enantiomer of racemic 1,2-epoxyhexane to afford a polycarbonate.[118]

In 2004, Darensbourg successfully described using **60** as a catalyst for the copolymerization of CO_2 and cyclohexene oxide in the presence of *N*-MeIm as a cocatalyst.[119] Since that early report, anionic cocatalysts, such as PPN^+Cl^- (PPN^+ = bis(triphenylphos-phoranediyl)ammonium cation), have proven to be more effective.[120] However, while the polymerization is efficient, traces of the highly colored salen Cr(III) complex in the product polymer lead to undesired color in the product polycarbonate. Since polycarbonate is not colored and its optical transparency is one of its important properties, procedures that easily separate the catalyst complex from the product polymers are of interest. Here we describe our research where we have explored the viability of liquid/liquid phase separation with a soluble polymer-bound catalyst as a way to address this issue.

We believed this problem could be addressed by using a nonpolar polymer such as polyisobutylene (PIB) as a support for salen Cr(III) complexes **59**. Since our prior success in using PIB-bound salen Cr(III) complexes **59** as a catalyst for ring opening of epoxides showed that **59** had similar reactivity profile as its low molecular weight counterpart **60**. We believed that a phase selectively soluble PIB group bound to a salen complex **59** could be used as a polymeric phase tag to prepare a catalyst that is like **60**

but that would be easily separable from the polycarbonate polymer that forms in reaction of cyclohexene oxide and CO_2 in CO_2.[121]

While polymerization catalysts are not always separated from their product polymers, there are a number of reports where polymer-bound polymerization catalysts including soluble polymer bound catalysts have been designed to be separated from a product polymer. For example, our group used a polyethylene-bound Nd carboxylate catalyst $(PE_{olig}CO_2)_3Nd$ in the polymerization of butadiene.[122] Polyethylene- and other soluble polymer-bound Cu(I) catalysts have also been used to separate Cu(I) from products in atom-transfer radical polymerization reactions.[46,50,123,124] Another more recent example described in a patent by Du Pont details the use of various soluble polymer-tethered porphyrin-like metal complexes as chain transfer catalysts to produce polyacrylates that are separated from the catalyst by a filtration or centrifugation after a monophasic polymerization reaction.[49]

The salen derivative **59** contains two polyisobutylated phenol groups and is phase selectively soluble in the heptane phase of a heptane/DMF, heptane/CH_3CN, or heptane/EtOH-H_2O biphasic mixture. This phase selective solubility was visibly high (Figure 4) and was quantified by UV-visible spectroscopy (λ_{max} = 350 nm, ε = 4514 M^{-1} cm^{-1}). In a biphasic heptane/90% EtOH-H_2O mixture < 0.001% of the starting complex **59** was in the polar phase. A photograph in Figure 4 illustrates the >99% phase selective solubility of **59** in a heptane/EtOH-H_2O biphasic mixture that was observed when a homogeneous equivolume heptane:EtOH solution of **59** was perturbed to from two phases by the addition of ca. 5 vol% H_2O.

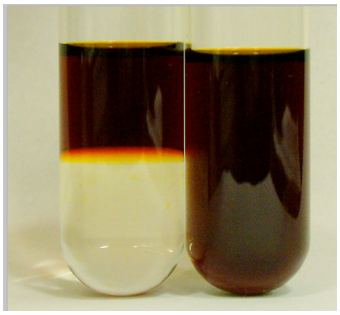
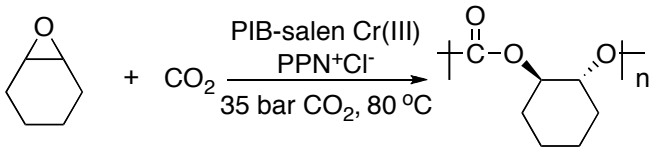


Figure 4. A photographic comparison of **59** in a biphasic mixture heptane/EtOH-H_2O solution and a monophasic mixture of heptane/EtOH.

In studies with the Darensbourg group, the polymerization of CO_2 and cyclohexene oxide was carried out in CO_2 at 80 °C as shown in eq. 55. The PIB-bound salen Cr(III) complex **59** or **60** and its cocatalyst PPN^+Cl^- were dissolved in dichloromethane for 30 min, then the solvent was removed by vacuum. The catalyst and cocatalyst were then redissolved in cyclohexene oxide, loaded into a Parr reactor, pressurized with 35 bar of CO_2, and heated to 80 ^oC. The reaction's progress was monitored using a ReactIR 1000 apparatus. Once the reaction was complete, the vessel was opened in air and allowed to cool. The product was dissolved in acetonitrile and acidified with conc. HCl. A heptane extraction removed most of the catalyst in the case of **59** (Figure 5a vs. 5b). A typical isolation procedure for **60** involved precipitation in acidic methanol to cleave the Cr(III) salen complex from the polycarbonate product. When the product solutions from a PIB-supported salen were compared to the product solutions formed using catalyast **60** there were obvious differences led to colorimetrically different products (Figures 5c and 5d). In this case, a less colored product was produced using catalyst **59**. Polycarbonate

prepared using **60** can be isolated, as an equally colorless solid but requires more precipitation steps.



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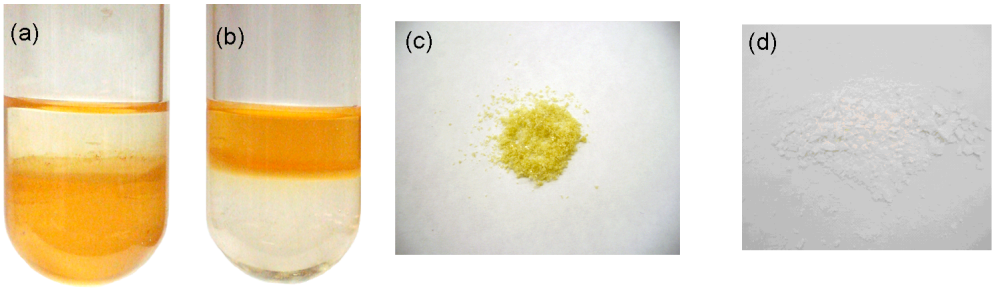


Figure 5. Colorimetric comparisons of a) a heptane/CH_3CN biphasic mixture of **60** and the product polycarbonate; b) a heptane/CH_3CN biphasic mixture of **59** and polycarbonate product; c) the polycarbonate formed using **60** isolated after one CH_3OH precipitation; and d) the polycarbonate isolated using **59** after one heptane precipitation.

The initial rate of polymerization by the salen Cr(III) complexes **59** and **60** is shown in Figure 6. These rates measured by *in-situ* IR spectroscopy are very similar. The similarity between the reaction profile of PIB-bound salen Cr(III) **59** While **59** can be completely separated from the polymer, recycling **59** led to a ca 20-30% lower polymerization rate. We believe this reflects the fact that the acidolysis step cleaves some Cr(III) from the PIB-salen complex **59**. Such Cr loss is seen both with **59** and with

60. In the case of **59**, the loss is substantially less than with **60** and with **59** ca. 4% of the starting Cr is lost in the product polymer phase based on ICP-MS analysis of the polycarbonate.

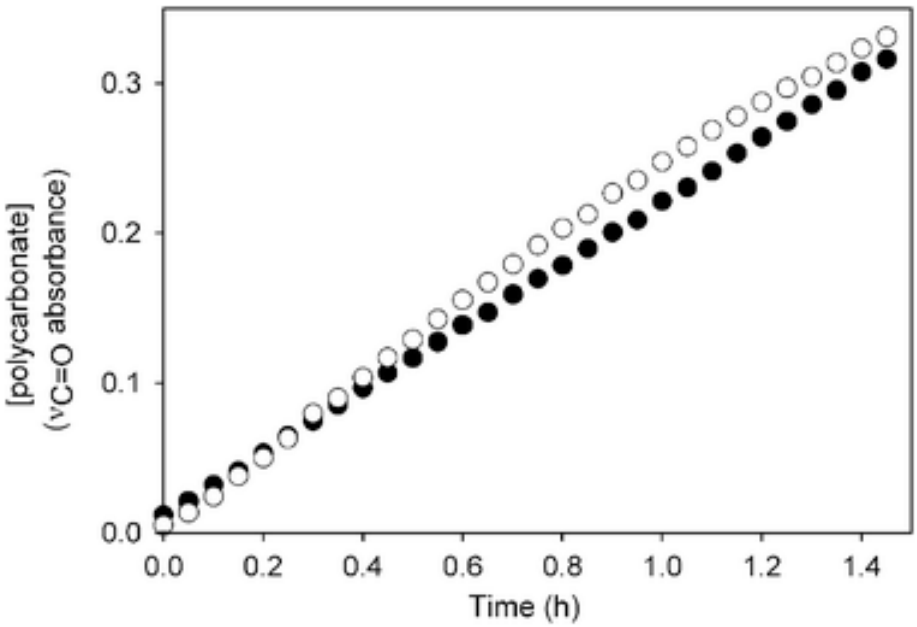


Figure 6. Initial rates for polymerization of cyclohexene oxide and CO_2 using either the PIB-salen Cr(III) complex **59** (o) or a low molecular weight analog **60** (●).

These results show that the PIB-bound salen Cr(III) complex **59** is an effective catalyst for the copolymerization of cyclohexene oxide and CO_2. The rate of polymerization catalyzed by **59** was very similar to its low molecular weight analog **60**. A control experiment using **60** under the same reaction conditions demonstrated that salen Cr(III) complex could not be separated from product polymers in a simple biphasic system without the polyisobutylene as a support (Figure 5a vs. Figure 5b). Figure 5c vs.

Figure 5d also showed the effectiveness of PIB as phase tag to separate product polymers from catalysts. Therefore PIB-bound catalyst is a useful but separable analog of these sorts of salen Cr(III) complexes.

Conclusions

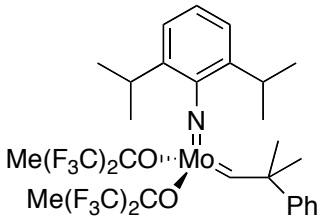
In summary, the studies in this chapter show that polyisobutylene oligomers are excellent nonpolar phase tags for chromophoric salen Cr(III) complexes. This phase tag facilitates separation of salen catalysts from products as shown in both ring opening of epoxides and polymerization of polycarbonate. This separation can be visually observed by the difference in color for the product polymer or product polymer phase as shown in Figure 5. The result from ICP-MS data also indicated only minimal amount of catalyst leaching. The synthesis of the salen complex bound to a PIB oligomer is straightforward. The synthetic products and the intermediates in the ligand synthesis can all be readily analyzed spectroscopically. The activity of the PIB-bound catalyst is similar to that of a non-supported catalyst, making it a useful but separable analog of these sorts of salen Cr(III) complexes.

CHAPTER III

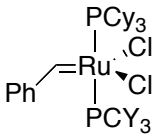
POLYISOBUTYLENE-SUPPORTED RING-CLOSING METATHESIS CATALYSTS

Introduction

Olefin metathesis is an alkylidene exchange reaction between two alkenes mediated by a transition-metal alkylidene complex.[125] While it is a relatively old reaction, more recent mechanistic insights have led the way for olefin metathesis to become a powerful synthetic tool for the formation of carbon-carbon double bonds.[6] This process allows chemists to efficiently synthesize an impressive range of molecules that only years ago required longer and more tedious synthetic routes.[126] The reaction is traditionally catalyzed by Schrock catalysts (**61**) like the Mo alkylidene complex[127] or a Grubbs catalyst (**62**) like the Ru benzylidene complex.[128] While both catalysts work, the commercially available 1st generation Grubbs catalyst **62** has many advantages over its Schrock catalyst counterpart.



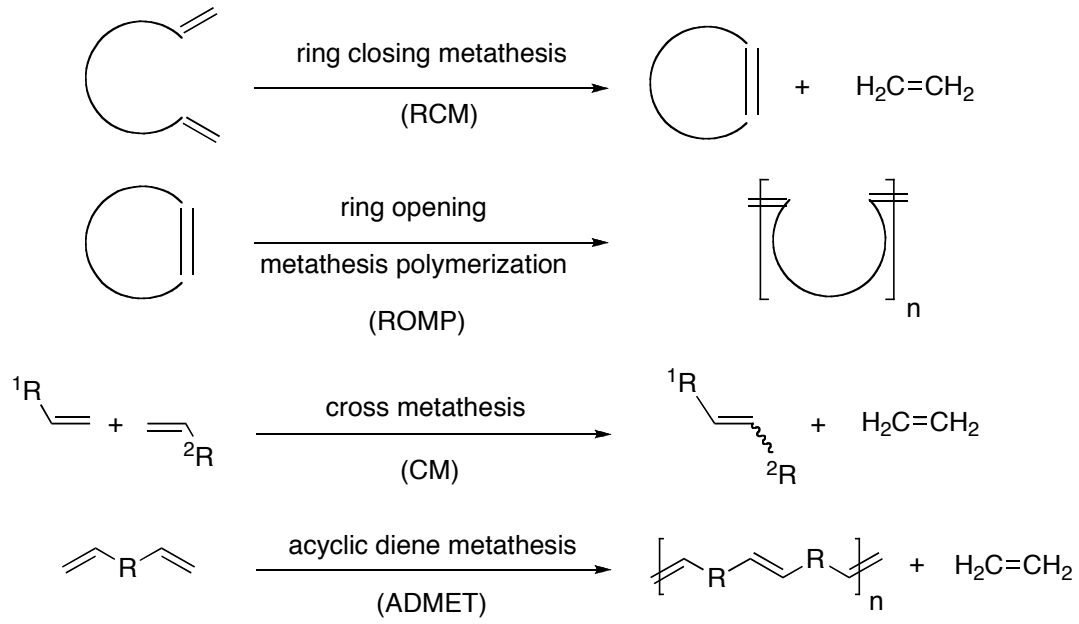
61



62

Catalyst **62** has been shown to be much more robust and possesses high tolerances to a wide range of functional groups than Schrock catalysts. The major drawbacks of a Schrock Mo-carbene complex are its high sensitivity to air, moisture, trace impurities present in solvents, and expense of preparation.[129] Because of these disadvantages, ruthenium-catalyzed ring-opening metathesis polymerization, cross metathesis, and acyclic diene metathesis polymerization are processes that are widely used in complex organic syntheses and in the formation of materials as shown in Scheme 4.[130-132]

Scheme 4. Examples of olefin metathesis.



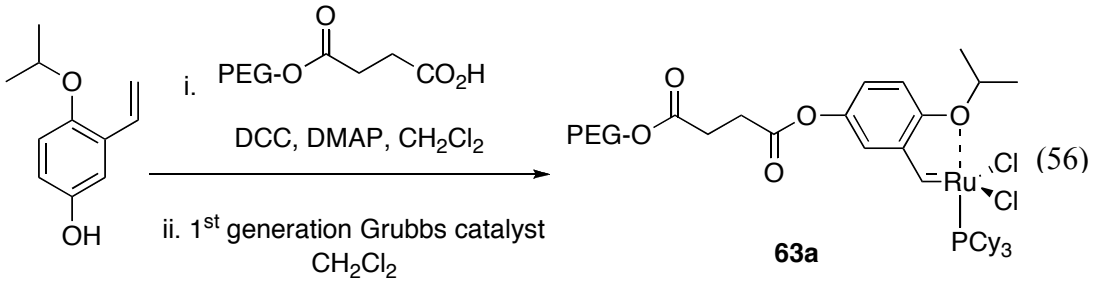
Ring-closing metathesis of dienes is an attractive and powerful synthetic tool for the formation of medium and large cyclic moieties ($\geq$ 5-member rings).[125] Smaller three- or four-membered ring and strained rings cannot be formed by ring-closing metathesis

because the ring-opening process is more thermodynamically favorable than ring closing. In fact, strained cyclic molecules such as norbornene derivatives are well-known substrates for ROMP reactions.[133] Cross-metathesis is the third type of metathesis process that provides a powerful synthetic tool for the preparation of an ever-increasing variety of complex biologically active molecules.[125] As in the case of dienes such as 1,5-hexadienes, the cross metathesis reaction can become a polymerization process known as acyclic diene metathesis polymerization or otherwise known as ADMET.[134] It should be noted that Grubbs catalyst (**62**) is only a precatalyst for the olefin metathesis process, but the active catalyst is a ruthenium-methylidene (**63b**). However for the simplicity of discussion, the term catalyst will be used for this dissertation.

While ruthenium-catalyzed olefin metathesis reactions have proven to be an attractive and powerful transformation for the formation of new carbon-carbon double bonds, only a limited number of industrial processes utilize ruthenium-based catalysts for olefin metathesis.[6] The principle exception to this is ROMP, which is usually used for the polymerization of bicycloalkenes like the cyclopentadiene dimer. This limited use of ruthenium-catalyzed olefin metathesis is perhaps surprising given its prominence and Nobel-prize status. While there may be several reasons why this powerful reaction is used mostly in the academic syntheses, the main reason is directly related to issues discussed previously in this dissertation dealing with the difficulty associated with removing ruthenium residues from the final products of a ring-closing or cross metathesis reactions.[6] A number of strategies used for the recovery and sequestration of

these ruthenium residues have been investigated. These include the use of soluble polymers, insoluble polymers, and boomerang insoluble polymer supported catalysts to deal with this issue.[135-141] Water and $scCO_2$ soluble ligands that enable catalysts use or recovery in environmentally benign or "green" solvents have also been developed.[142,143] In addition, ionic liquids have also been used to immobilize and recover ruthenium-based catalysts.[144,145] Since the main focus of this dissertation is the use of homogeneous supports, only some of these examples that use soluble polymer supported ruthenium-based olefin metathesis catalysts will be discussed below. This discussion serves as a prelude to the discussion of my work in Bergbreiter's laboratory that has led to recoverable and heptane soluble ruthenium metathesis catalysts.

The immobilization of a Hoveyda-type catalyst onto a polyethylene glycol or PEG was first reported by Yao in 2000.[146] In this report, the homogeneous PEG-bound 1st generation Hoveyda-Grubbs catalyst **63a** was synthesized as shown in eq. 56. With 5 mol% catalyst, the polymer supported complex **63a** was recycled through eight cycles in the ring-closing metathesis reaction of dienes. Upon completion of a ring-closing metathesis reaction in dichloromethane, catalyst **63a** could be recovered by solvent precipitation into diethyl ether. The gradual decrease in yield from 98% in the first cycle



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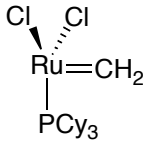
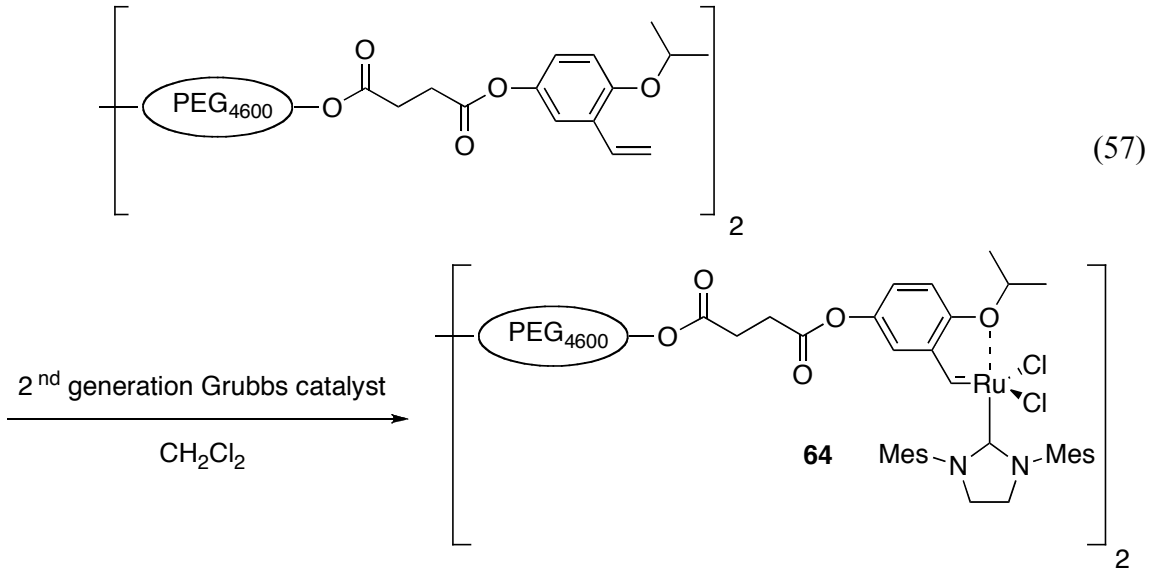


63b

to 92% in the eighth cycle was attributed to the decomposition of a monophosphane-based ruthenium carbene (**63b**), which formed during the catalytic cycle.[147] In an attempt to improve upon **63a**, Yao and Motta reported a new catalytic system that involved attaching two ruthenium complexes onto PEG, as shown in eq. 57.[148] This new PEG-bound 2nd generation Hoveyda-Grubbs catalyst **64** proved to be highly reactive and much more recyclable than **63**. As a catalyst for ring-closing metathesis reaction, **64** could be reused up to 17 cycles for a wide variety of dienes, including the formation of tetrasubstituted olefins (eq. 58). The level of ruthenium leaching was not reported in either study.



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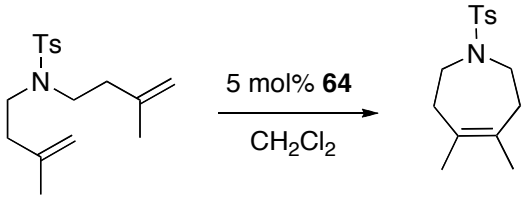
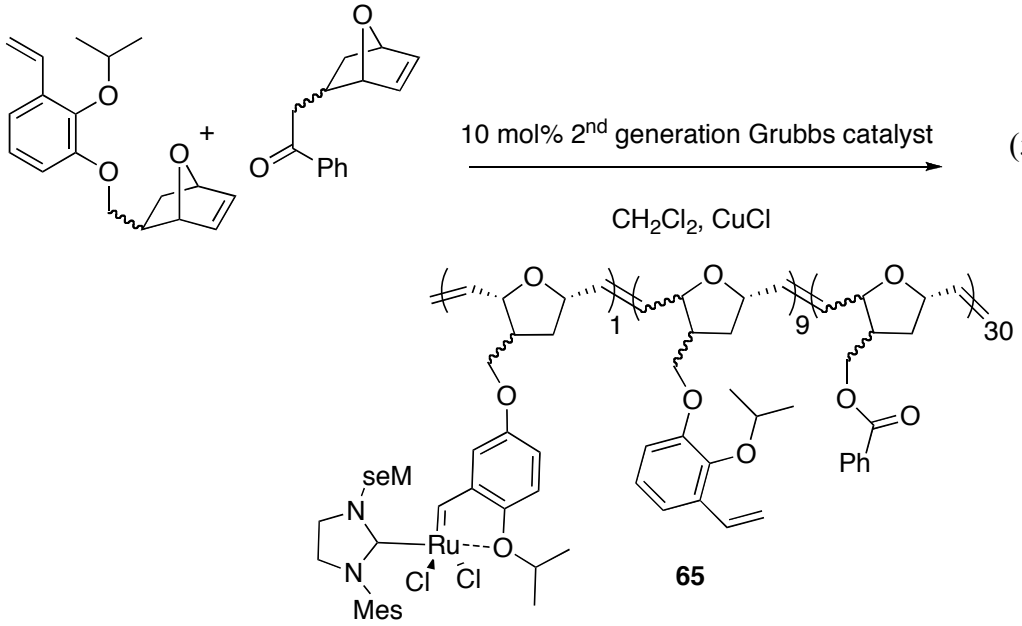


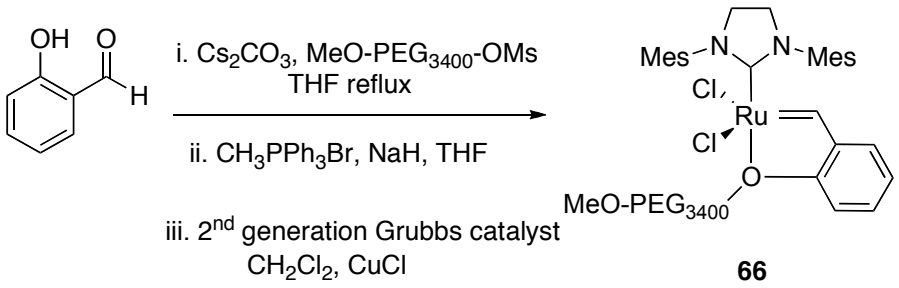
(58)

In 2002, Blechert and coworkers reported the synthesis of polyfuran-supported 2nd generation Hoveyda-Grubbs catalyst **65** (eq. 59).[137] The soluble polymeric ruthenium complex **65** could efficiently catalyzed ring-closing metathesis reaction with catalyst loadings as low as 1 mol%. Catalyst **65** could be recovered by solvent precipitation in either hexane or diethyl ether and could be reused up to eight times without any decrease in reactivity. The total-reflection X-ray fluorescence (TXRF) analysis of the products, after catalyst separation, indicated that a maximum of 0.004% ruthenium leaching in each of the first four cycles.



(59)

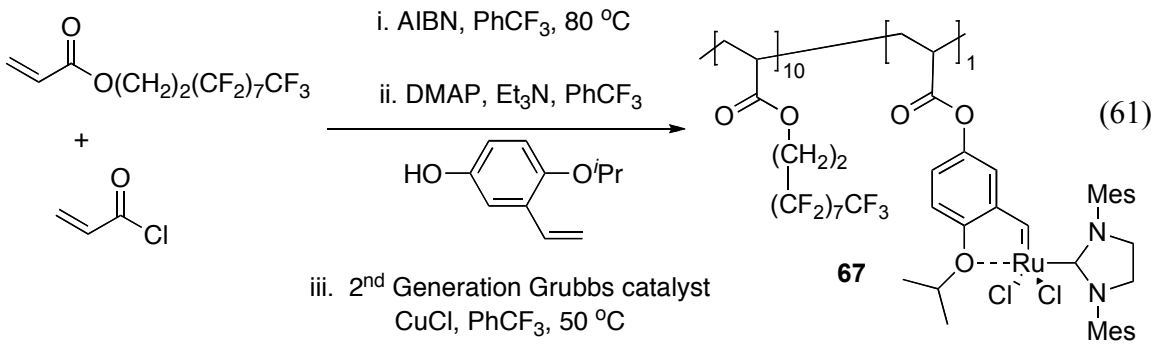
In 2003, Lamaty and coworkers described the synthesis of PEG-supported 2nd generation Hoveyda-Grubbs catalyst **66** in which the polymer was attached through the ether fragment of the benzylidene ligand (eq. 60).[149] However, an unusually high level of catalyst (10 mol%) was necessary to promote ring-closing metathesis reactions. Catalyst **65** could be recovered by solvent precipitation into diethyl ether. A significant loss of reactivity was observed in recycling studies as yields decreased to 85% in the fourth cycle. The level of ruthenium contaminations in products was not reported.



(60)

Yao and Zhang developed a fluorous polymer supported 2nd generation Hoveyda-Grubbs catalyst **67** for use in fluorous biphasic media.[141] A metathesis catalyst **67** with a Grubbs-Hoveyda Ru complex as a pendant group on a fluorinated acrylate was synthesized as shown in eq. 61. They then used this polymer-bound catalyst **67** in ring closing metathesis of 1,6- and 1,7- diene substrates in a mixture of $PhCF_3$ and CH_2Cl_2(1:19, v/v) at 50 ºC. They noted that this catalyst could be completely recovered by a post-reaction extraction with a fluorinated solvent (FC72) due to its excellent solubility in fluorous solvents. The level of ruthenium contaminations in products was not reported. However, the level of ruthenium contaminants in the product phase was

assumed to be very low due to high percent conversions and the recyclability of **67** through 20 reaction cycles.



(61)

Results and Discussion*

Here we describe an alternative approach of the recovery of Ru-metathesis catalyst using a heptane-soluble polymer (PIB) to prepare a 2nd generation Hoveyda-Grubbs catalyst that is recoverable and reusable in hydrocarbon solvents by liquid/liquid or liquid/solid separations after catalysis.[150] Two strategies are possible with a heptane-soluble catalyst. First, a catalyst selectively soluble in a heptane rich phase of a liquid/liquid biphasic mixture can be recovered in that phase after a monophasic reaction. This can be done using thermomorphic, latent biphasic conditions, or by product extraction with a heptane-immiscible solvent.[59,60] A second approach is to simply carry out the reaction in heptane and to rely on the fact that many polar organic products are not especially soluble in heptane. If such a product were a solid, a simple

* Reprinted with permission from "Heptane-Soluble Ring-Closing Metathesis Catalysts" by Hongfa, C.; Tian, J.; Bazzi, H. S.; Bergbreiter, D. E. *Org. Lett.* **2007**, *9*, 3259, Copyright 2007 by the American Chemical Society.

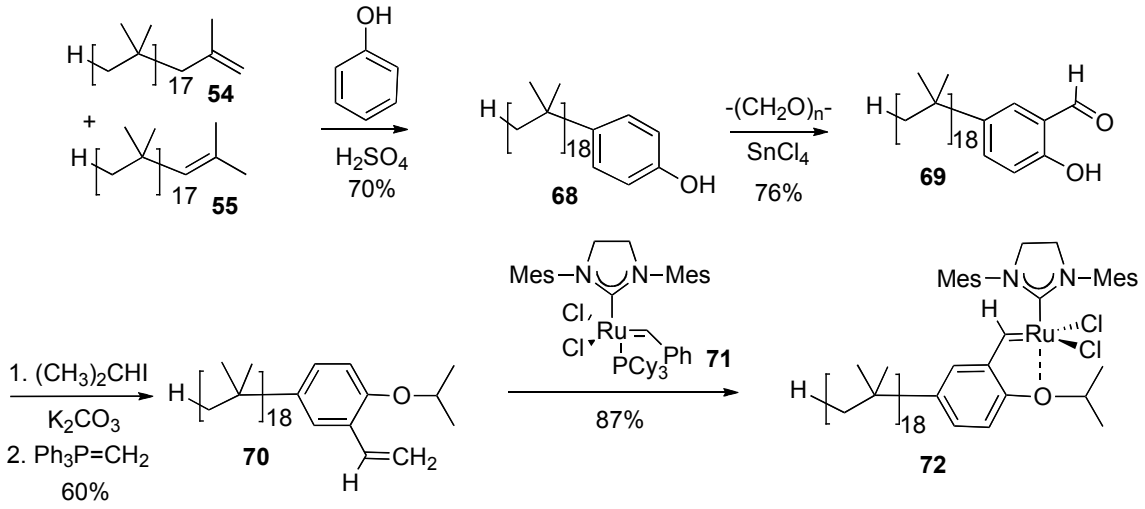
filtration or decantation can then separate the catalyst and the precipitated product. Both approaches are described below.

The general strategy for synthesis of a heptane-soluble metathesis catalyst relied on the use of commercially available vinyl-terminated polyisobutylene. While this material can be >90% $=CH_2$ terminated polyisobutylene **54**, some samples contain as much as 20% of the internal double bond (e.g. polyisobutylene **55**). However, a Friedel-Crafts alkylation of either structurally isomeric polyisobutylene oligomer yields the same 4-(polyisobutyl)phenol product **68**.[99] Formylation of this oligomeric phenol using paraformaldehyde produces the 2-hydroxy-5-(polyisobutyl)benzaldehyde **69**. This product can in turn be converted into the oligomeric styrene derivative **70** using a Wittig olefination. Exchange of the methylene group with the benzylidene group of the commercially available 2nd generation Grubbs catalyst **71** produced the desired heptane-soluble catalyst **7**2 (Scheme 5). The last step of this synthesis also used flash column chromatography to separate the PIB-bound Ru complex **72** from starting materials. Chromatography is not usually used in synthesis of polymer-bound catalysts but is feasible for **72** just as it is feasible for PEG-bound or dendrimer-bound catalysts.[136,142]

As is the case for other terminally functionalized polymer-bound ligands/catalysts, all of the intermediates in these syntheses could be characterized by simple solution state ^{1}H-NMR spectroscopy.[8,99,151] Figure 7 illustrates the sort of ^{1}H-NMR spectra that can be obtained for species like catalyst **72**. This spectrum establishes that the catalyst **72**, like its low molecular weight analog, involves the isopropyloxy group in the Ru coordination

sphere as the heptet due to the CH of the isopropyloxy shifts from δ 4.51 in **70** to δ 4.87 in **72** (cf. Figure 7 insets a and b).

Scheme 5. Synthesis of a PIB-supported 2nd generation Hoveyda-Grubbs catalyst.



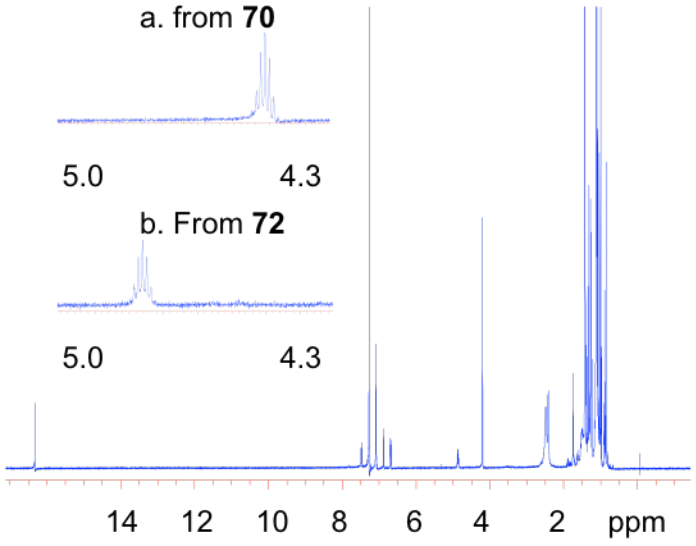


Figure 7. ^{1}H-NMR spectrum of a PIB-bound ruthenium metathesis catalyst **72** showing changes in the *i*-Pr heptet in inset a and b for **70** and **72** respectively.

Other than having a polyisobutylene-containing ligand that makes it heptane soluble, the catalyst **72** was unexceptional in its reactivity, converting a variety of α,ω-dienes into cyclic olefins at room temperature (Table 2). The catalyst could be recycled multiple times. The recycling of **72** was accomplished several ways. The most standard approach used for dienes like **73** and **81** involved carrying out the reaction in heptane and then extracting the product using acetonitrile. In such cases, the less dense heptane phase contained catalyst **72** and recycling simply involved addition of fresh substrates.

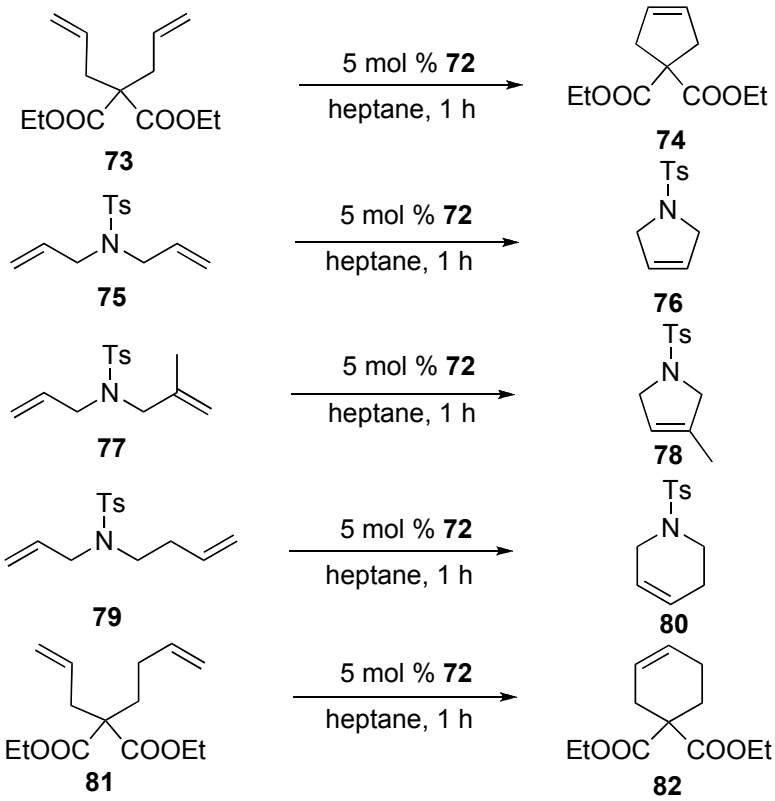
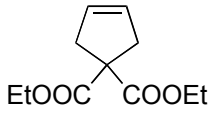
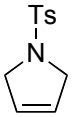
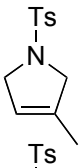
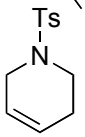
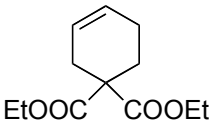


Table 2. Ring-closing metathesis reactions with catalyst **72**.

product	cycle 1	cycle 2	cycle 3	cycle 4	cycle 5
	66%	75%	75%	94%	99%
	72%	81%	94%	98%	98%
	84%	84%	93%	99%	99%
	67%	76%	84%	84%	93%
	62%	70%	80%	88%	96%

Yields in cycle 1-5 are of products isolated by solvent removal and increase cycle to cycle because of saturation of the heptane phase by products.

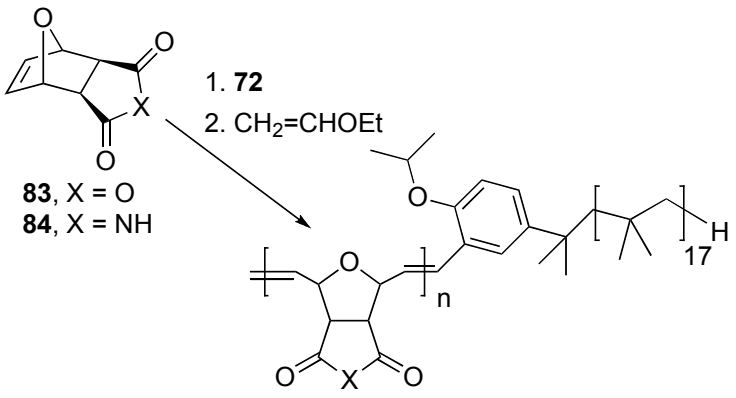
While catalyst **72** was in our experience, equivalent in reactivity to the commercially available **71**, its good solubility in heptane and the generally poor solvating ability of heptane toward many polar organic products makes another recycling scheme possible. For example using the substrates **75, 77,** and **79** in Table 2, we were able to carry out the reaction through at least five cycles by simply adding a heptane-soluble starting material to the heptane solution of the catalyst. After 1 h, the heterocyclic product precipitates from heptane leaving a solution of the catalyst that can

be separated by forced siphon and reused. The apparent increases in yields from cycle 1-5 in Table 2 reflect saturation of the heptane phase by products.[94,100] If a catalyst were used through multiple cycles this would pose little problem unless the product or byproducts were heptane soluble.[152]

The efficiency of separation of catalyst and product was evaluated by ICP-MS analysis using a sample of product **74** and **76** from the 1st and 3rd reaction cycles of a cyclization like that of Table 2. Combustion of the product and digestion of any residue in concentrated sulfuric acid showed the presence of ca. 20 ppm Ru in the product phase. This translates to a recovery of ca. 97% of the Ru for the second cycle. The loss of Ru presumably reflects the fact that the present scheme requires that the Ru-methylidene intermediate formed from **72** is to be recaptured by **70**, which is formed *in situ,* for complete Ru recovery. Inefficiencies in this process and loss of Ru to another phase are most notable in the higher level of Ru contamination in experiments where **76** precipitated from heptane. In this case, ca. 96% of the Ru catalyst was still recovered, but the solid product contained ca. 1000 ppm of Ru. This high concentration of Ru is due the small volume of the product phase and partitioning of Ru species onto the small volume of the polar solid that is formed. This suggests that designing other systems where the Ru species that are involved in the catalytic cycle always have a hydrocarbon soluble ligand may lower Ru leaching. In the next chapter, this type of system will be discussed as a way to improve upon PIB-bound ruthenium catalyst.

The reactivity of catalyst **72** was also tested in the ring opening-metathesis polymerization (ROMP) reaction.[133,152] In this case, the use of **72** is expected to generate

amphiphilic block copolymer, since the mechanism of ROMP requires that the benzylidene ligand's PIB chain must be incorporated at the end group of the polymer chain. The ROMP reactions of **83** and **84** with catalyst **72** were studied in THF at room temperature (eq. 62) using a monomer:initiator ratio of 30:1. ^{1}H-NMR spectroscopy showed quantitative conversion of the monomer occurred in both reactions after 20 min. The reactions were then quenched with ethyl vinyl ether, and the resulting polymers were isolated. These results show that catalyst **72** is thus useful both in RCM or ROMP chemistry.



(62)

Conclusions

The studies in this chapter show that terminally vinyl-functionalized polyisobutylene oligomers can be easily transformed into PIB-bound ruthenium metathesis catalyst precursors. The nonpolar catalyst so prepared can be used in solvents such as heptane and can be recycled by a simple gravity-based extraction after addition of heptane-immiscible polar solvent such as acetonitrile. The alternative

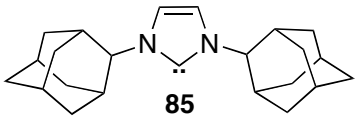
method of separation involves the precipitation of products from the heptane rich phase containing catalysts. The synthesis of a PIB-supported 2nd generation Hoveyda-Grubbs catalyst could be easily monitored by conventional spectroscopy. The activity of the PIB-supported catalyst **72** is analogous to that of other soluble polymer supported catalysts or their non-supported analogs. However, the level of ruthenium contamination was very high (ca. 1000 ppm) in comparison to the strategies that were reviewed earlier in this chapter. In the next chapter, I describe how we improved on the use of this PIB-bound 2nd generation Hoveyda-Grubbs catalyst precursor by moving the PIB phase solubility anchor from the benzylidene ligand to the *N*-heterocyclic carbene in order to keep the support attached to the catalyst throughout the whole catalytic cycle.

CHAPTER IV

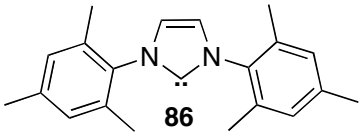
POLYISOBUTYLENE-SUPPORTED *N*-HETEROCYCLIC CARBENES

Introduction

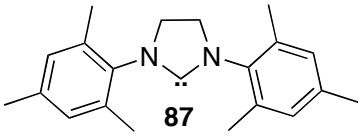
The first report of an *N*-heterocyclic carbene (NHC) was published in 1961 by Wanzlick[153] and followed by several reports of the synthesis of metal carbene complexes by Öfele[154], Wanzlick[155], and Lappert[156-159] in the late 1960s and early 1970s. These articles reported the synthesis of a five-membered ring *N*-heterocyclic carbene that was able to form complexes with a variety of metals. Many of the earlier works by Lappert and coworkers showed promising results, but the inherent instability of *N*-heterocyclic carbenes caused a major problem for the use of these new ligands. It was not until two decades later that the first synthesis of a stable *N*-heterocyclic carbene **85** (1,3-di-1-adamantyl-imidazol-2-ylidene) was realized by Arduengo.[160] The success of Arduengo and coworkers led to the synthesis of 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene **86** or IMes[161] and 1,3-bis(2,4,6-trimethylphenyl) imidazolin-2-ylidene **87** or SIMes.[162]



85



86

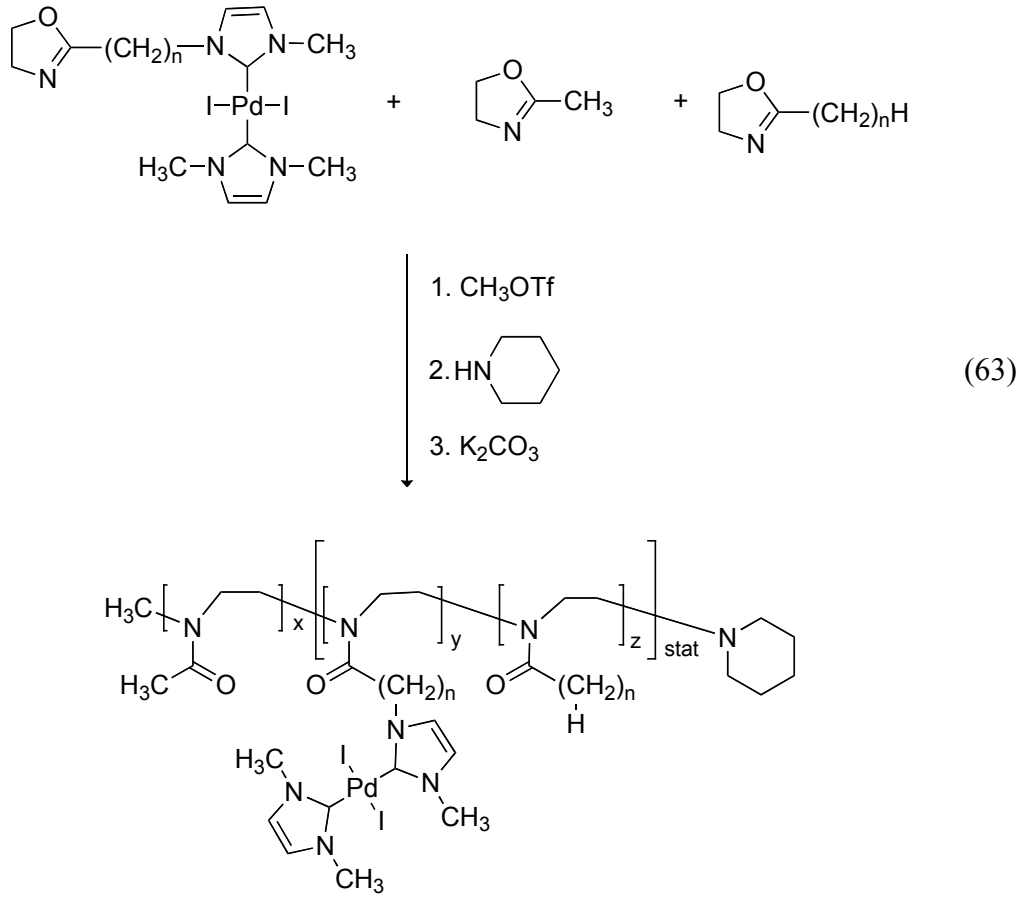


87

The breakthrough by Arduengo and coworkers revived interest in these new ligand species. Since 1991, NHCs have become universal ligands for a wide variety of organometallic complexes that can be utilized as catalysts for a spectrum of reactions.[163,164] NHCs are electron-rich, neutral strong σ-donors, but poor π-acceptor ligands that are able to bind strongly to the metal center with little tendency to dissociate from it.[163] This particular class of ligand also has greater thermal and air stability than phosphines.[164] Therefore, the use of nucleophilic *N*-heterocyclic carbene is an attractive alternative to phosphine ligands. NHCs by themselves are also attractive as organocatalysts that have a long history and are analogous to biological catalysts.[165] The versatility of NHCs as ligands and catalysts has led to growing interests in tethering this type of carbene onto a variety of supports, including soluble/insoluble polymers.[164] Since the theme of this dissertation is the use of homogeneous supports, only some of the examples that use soluble polymer supported *N*-heterocyclic carbene ligands will be discussed below as a prelude to a discussion of my work in Bergbreiter's group that has led to polyisobutylene-anchored *N*-heterocyclic carbene ligands.

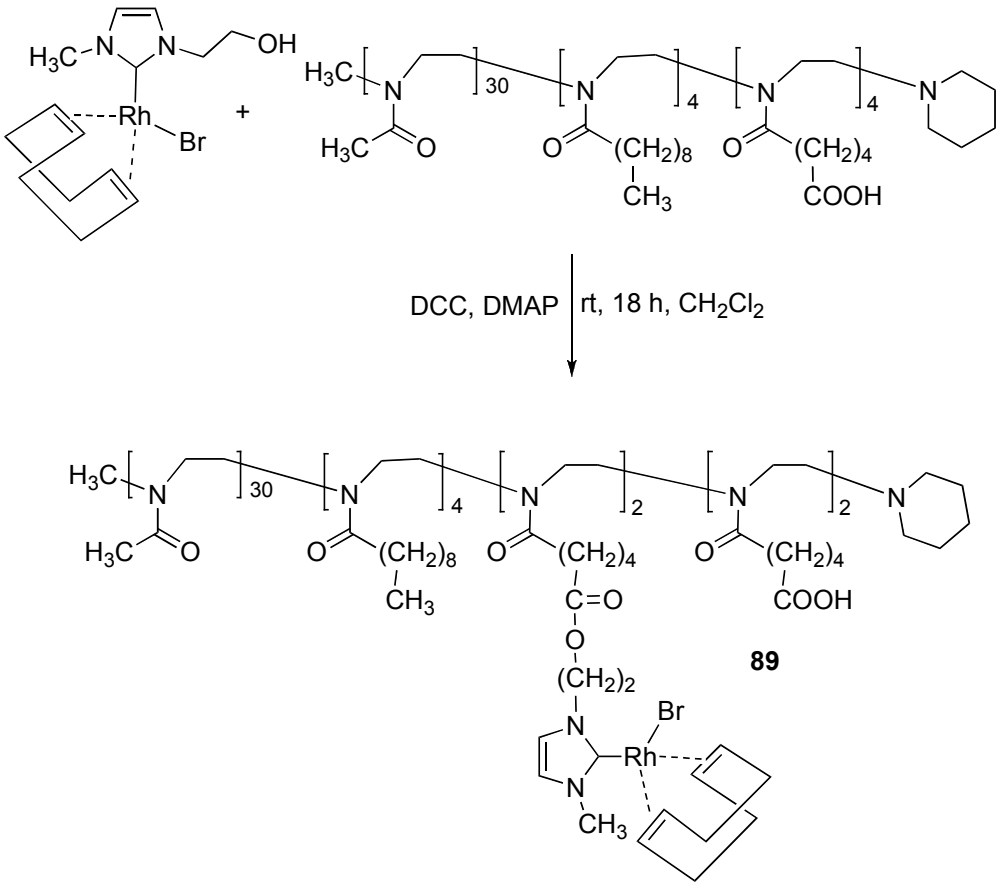
Weberskirch's group reported a series of publications where poly(2-oxazoline) copolymers were used to separate, recover, and recycle cross-coupling Pd-NHC catalysts[166,167] or Rh –NHC hydroformylation and hydrogenation catalysts.[168] Poly(2-oxazoline) copolymer-bound Pd-NHC (**88**) and Rh-NHC (**89**) catalysts were prepared as shown in eq. 63 and 64.[167,168] In these examples, the metal ligation involved an *N*-heterocyclic carbene ligand and the polymers were prepared using a Pd-complex as a

comonomer or by a post-polymerization coupling of a Rh complexed functional NHC ligand to a pendant -CO_2H group.



(63)

88a: n = 4; x = 28; y = ca. 2; z = ca. 3 M_n = 3920 g/mol
88b: n = 6; x = 29; y = ca. 2; z = ca. 3 M_n = 4400 g/mol
88c: n = 8; x = 30; y = ca. 2; z = ca. 3 M_n = 4730 g/mol



(64)

Unlike PEG, these amphiphilic block copolymer-supported catalysts were not completely soluble in water. Instead, these amphiphilic polymers formed micellar aggregates with a 15-nm hydrodynamic radius under the reaction conditions. The polymer-bound Pd catalyst **88a-c** showed good catalytic activity in the coupling of iodobenzene and styrene. For example, ca. 93% of *trans*-stilbene was obtained after 3 h at 90 ºC using 0.67 mol% catalyst for **88a**, **b**, or **c**. In these cases, the spacer length affected the catalytic activity of the pendant polymer-bound catalysts. A minimum spacer length of six methylene groups was needed to reach the highest turnover frequency (TOF = 570 h^{-1}). This is consistent with NMR spectroscopic studies of

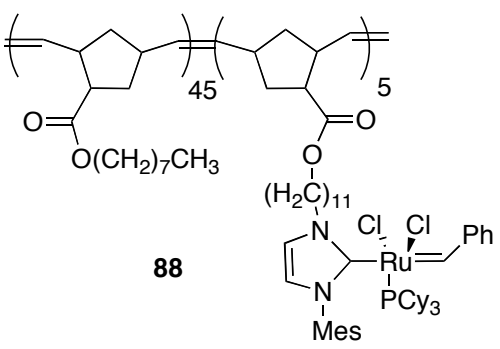
pendant groups on other water soluble polymers that showed spaces of this size confer rotational freedom on attached groups.[77] Recycling of catalyst **88c** was performed by a post reaction extraction with diethyl ether. The initial yield of 80% in the first cycle reduced somewhat to 68% in the third cycle. While the authors speculated that the lower activity might arise from residual diethyl ether left in the aqueous phase that prevented the solubilization of the substrates, other explanations such as catalyst decomposition or metal leaching for a decreased rate were not fully explored. The same catalyst used in Heck couplings was also effective in the Suzuki coupling reactions between iodobenzene and phenyl boronic acid. The highest TOF number (5200 h^{-1}) was achieved by using 0.1 mol% of catalyst **88c** at 80 ºC. In this case no results on catalyst recycling were reported.[167]

The rhodium catalyst **89** was successfully reused four times in the hydroformylation of 1-octene under aqueous biphasic conditions using a mixture of water and 1-octene where the substrate 1-octene was the organic phase. The organic phase consisting of the aldehyde products was separated by decantation after the reaction and the denser aqueous catalyst-containing phase was directly reused in the next cycle. Rh leaching into the product phase after the first cycle was measured by ICP-OES (inductively coupled plasma-optical emission spectroscopy). The TOF varied from 1100 h^{-1} to 2350 h^{-1} in the third cycle to 2360 h^{-1} in the fourth cycle. These TOF values were similar to those seen for an analogous low molecular weight analog in benzene (TOF = 2400 h^{-1}) measured in the same lab with a structurally similar Rh-carbene catalyst. The authors suggested that the initially lower TOF number in the first two cycles and variation of the *n*:*iso* ratio

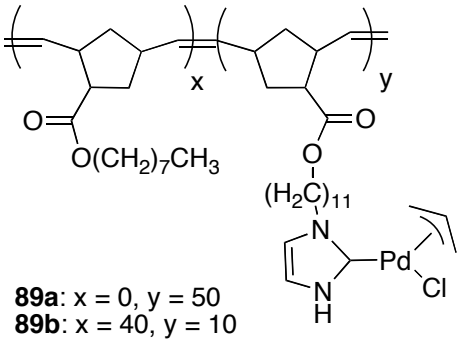
from 2.6 in the first cycle to 1.2 in the last two cycles were due to incomplete exchange of the bromide on rhodium for hydride in the initial cycles. Analyses for bromide in the recovered catalysts that would have established this were not reported. The authors also noted some hydrolysis of the ester group that coupled the Rh-NHC complex to the polymer in **89** occurs over 18 h. This resulted in a calculated loss of 2.7% of the charged Rh in each 2 h reaction cycle.

Weck and Sommer described the synthesis of poly(norbornene) supported 2nd generation Grubbs (**88**) and Pd-NHC complexes (**89-91**).[169] Weck utilized the ring-opening metathesis polymerization chemistry with a 1st generation Grubbs catalyst as a route to polynorbornene-supported NHC ligands where the concentration density of the carbenes in the polymer was controlled by the presence or absence of a comonomer. The catalyst activity of **88** was tested on the ring-closing metathesis of diethyl diallylmalonate in dichloromethane at 45 ^{o}C. Under these conditions, the diethyl diallylmalonate was converted in 95% yield to its corresponding RCM product. Catalyst **88** was recovered by precipitation in cold methanol, but was not recycled. Elemental analysis of the reaction solution after the removal of **88** showed no detectable amount of ruthenium remained in solution, which indicated the quantitative removal of catalysts from products. The catalytic activities of **89-91** were tested in the Sonogashira, Suzuki, and Heck reactions. Good overall yields greater than 90% were reported when using activated and non-activated aryl halides for all three reactions. Catalyst **90a** was shown to be the most active catalyst. However, the formation of palladium black was observed during the Heck coupling of iodobenzene and *n*-butyl acrylate. The recycling

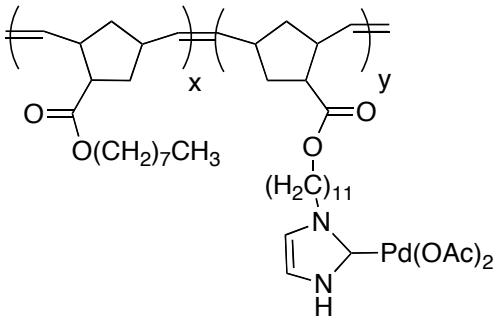
experiment was carried out with the Suzuki-Miyamura coupling of chlorobenzene with phenylboronic acid. After the reaction was complete, the reactants and products were distilled off and the resulting polymeric residue was dried. The polymeric residue was reused for two more cycles but the conversion decreased drastically from 80% in the first cycle to 44% in the third cycle.



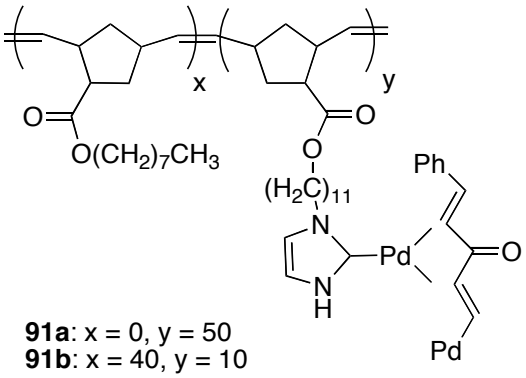
88



89a: x = 0, y = 50
89b: x = 40, y = 10

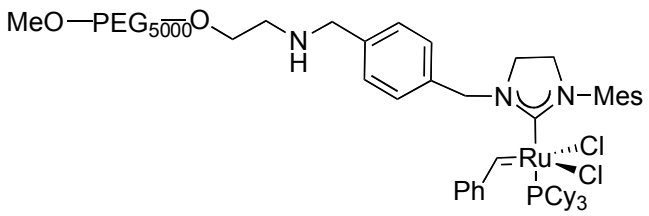


90a: x = 0, y = 50
90b: x = 40, y = 10



91a: x = 0, y = 50
91b: x = 40, y = 10

As mentioned earlier in this dissertation, the ruthenium-catalyzed olefin metathesis is a powerful method for carbon-carbon bond formation. The stability and versatility of this sort of catalyst had allowed Grubbs and coworkers to develop a water- soluble



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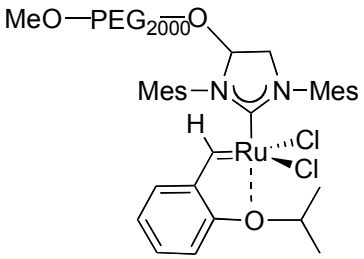
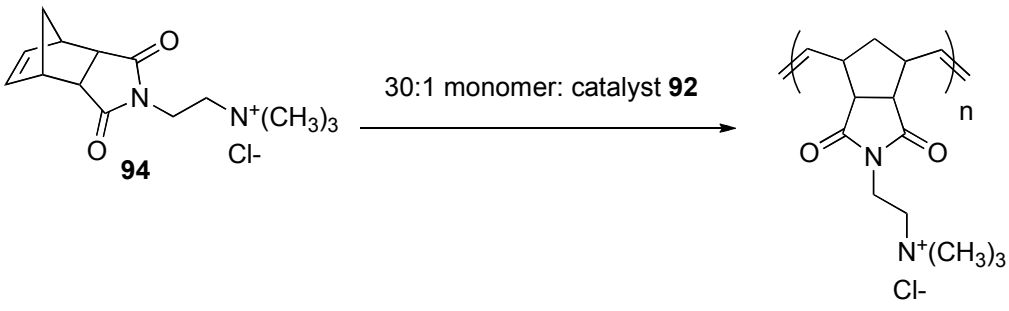


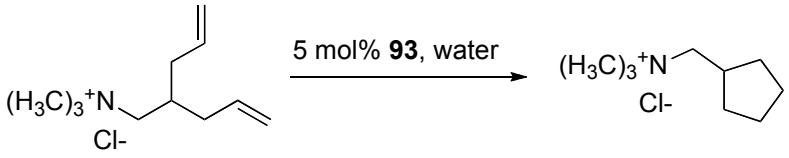
93

metathesis catalyst. In 2005, Grubbs utilized PEG as a support in the synthesis of a Grubbs 2nd generation catalyst (**92**).[170] This was the first example of PEG as a homogeneous water-soluble support for NHC that was then used as a ligand for Grubbs catalyst.[170] The catalyst **92** so formed was shown to be highly active for the ring-opening metathesis polymerization of water-soluble *exo*-monomers **94** (eq. 65).

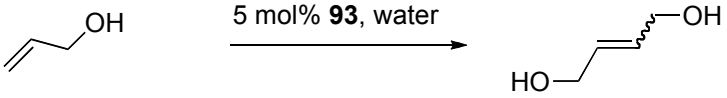


94 (65)

However **92** was unable to mediate the ring-closing metathesis reaction of α,ω-dienes in water and showed only limited reactivity in methanol. In order to improve upon **92**, Grubbs and Hong synthesized a PEG-bound 2nd generation Grubbs-Hoveyda catalyst (**93**).[142] A PEG-bound ruthenium catalyst **93** was very active for the ring-closing metathesis reaction for water soluble α,ω-dienes as shown in eq. 66. Cross-metathesis was also tested in water and was also successful with >94% conversion of allyl alcohol to 1,4-dihydroxybut-2-ene as shown in eq. 67. Grubbs and Hong utilized the water-soluble nature of **93** could be used as a handle to remove ruthenium byproducts from products by simple aqueous extraction.[171]



(66)



(67)

Results and Discussion

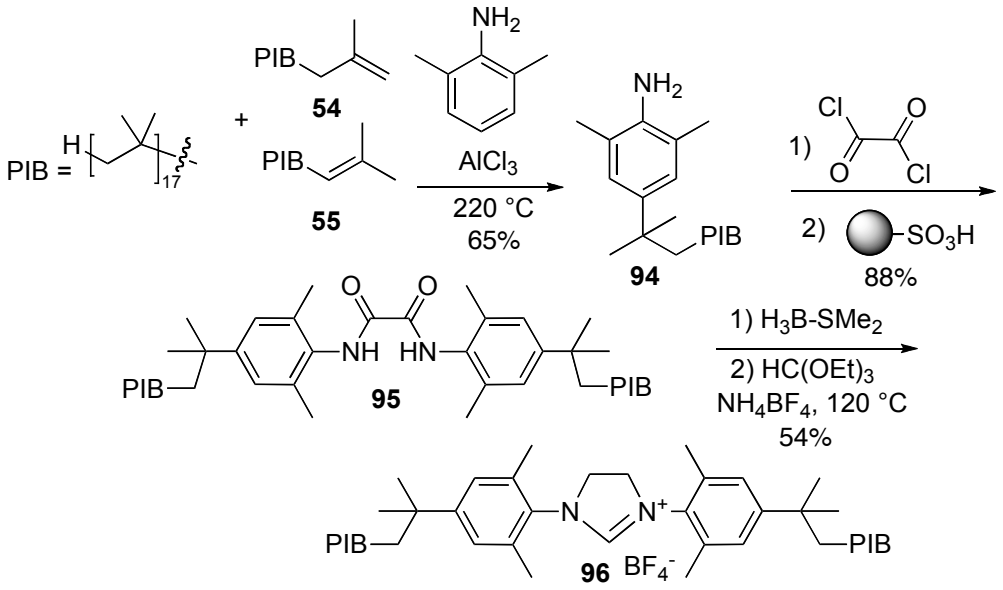
As mentioned earlier in the discussion of this chapter, *N*-heterocyclic carbenes have become widely used ligands for organometallic chemistry since Arduengo's initial report.[160] While their use in metathesis chemistry is most common, metal complexes derived from these structurally diverse ligands are useful in many catalytic processes.[172]

Thus, there is significant interest in strategies that facilitate separation, recovery and reuse of these ligands and their metal complexes. Some of the examples of these strategies were discussed in the introduction to this chapter. Below we describe new routes to recoverable, heptane-soluble NHC ligands and their use as supports for recoverable, reusable metathesis catalysts.

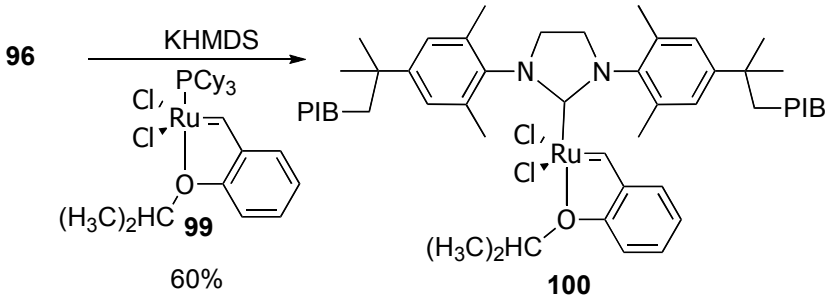
Insoluble cross-linked polymers or inorganic supports for recoverable reusable NHC-ligated metal complexes useful in catalysis are known.[6] Examples of soluble polymer supports for these catalysts too have been described, but these latter reports are limited to the use of poly(ethylene glycol) (PEG) supports.[6,173] PEG supports attached to an imidazolium carbon or to an imidazolium nitrogen yield NHC catalysts that are water-soluble and recoverable by solvent precipitation. Here we describe using heptane-soluble polyisobutylene as phase anchors[99] to prepare separable NHC metal complexes. As shown below, PIB groups can be attached to these carbene precursors and the product PIB-bound NHCs form metal complexes that are phase selectively soluble in the heptane phase of thermomorphic mixtures of heptane and polar solvents. Alternatively heptane solutions of these NHCs can be extracted with polar solvents with minimal losses of the metal complex. This behavior is demonstrated both for Ag(I) complexes and with separable, recoverable, and reusable Ru catalysts that can be used for ring closing metathesis reactions.

Three approaches were explored to synthesize PIB-supported NHC ligands. First, a Friedel-Crafts alkylation of commercially available mixture of alkene-terminated PIBs **54** and **55** afforded 2,6-dimethyl-4-(polyisobutyl)aniline **94** which like mesityl amine

Scheme 6. Synthesis of the PIB-SIMes Salt **96** from polyisobutylene.

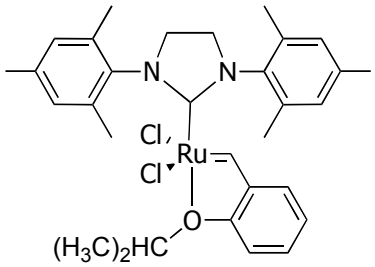


reacts with oxalyl chloride to form the diamide **95**. This amidation reaction used excess **94** which was separated from the diamide product using an Amberlyst resin as a scavenger.[174] The diamide product was then reduced to form a diamine that was converted into the PIB-bound imidazolium tetraborofluorate salt **96** using known chemistry (Scheme 6).[142] The formation of metal complexes from the imidazolium salts



(68)

used KHMDS to deprotonate **96** to synthesize a PIB-supported Hoveyda-Grubbs 2nd generation catalyst **100** from the Hoveyda-Grubbs 1st generation catalyst **99**[142] as shown in eq. 68. The PIB-bound ruthenium complex **100** had ^{1}H and ^{13}C-NMR spectra that were similar to those of its low molecular weight counterpart (**101**).



101

A UV-visible spectroscopy analysis showed a heptane phase selective solubility difference of 99:1 versus 1:100 for **100** vs. **101** in a thermomorphic equivolume mixture of heptane and CH_3CN. This >1000-fold difference is evident in a visual comparison (Figure 8) and by ICP-MS analyses that showed a 97:3 versus a 1:99 phase selective solubility for **100** and **101** in the heptane phase of a heptane/CH_3CN mixture. As noted in Chapter III and in the catalyst study below, the ruthenium leaching is lower than three percent. This number may be due to the residual amount of **99** in the product **100** as a result of an incomplete reaction. The loss of ca. 3% ruthenium to the CH_3CN phase can be considered to be an upper limit for the amount of ruthenium that might leach into a product phase.

Figure 8. Visually evident phase separation of **100** and **101** a) a heptane/acetonitrile mixture; b) a heptane/DMF mixture; c) a heptane/EGDA (ethylene glycol diacetate) mixture.

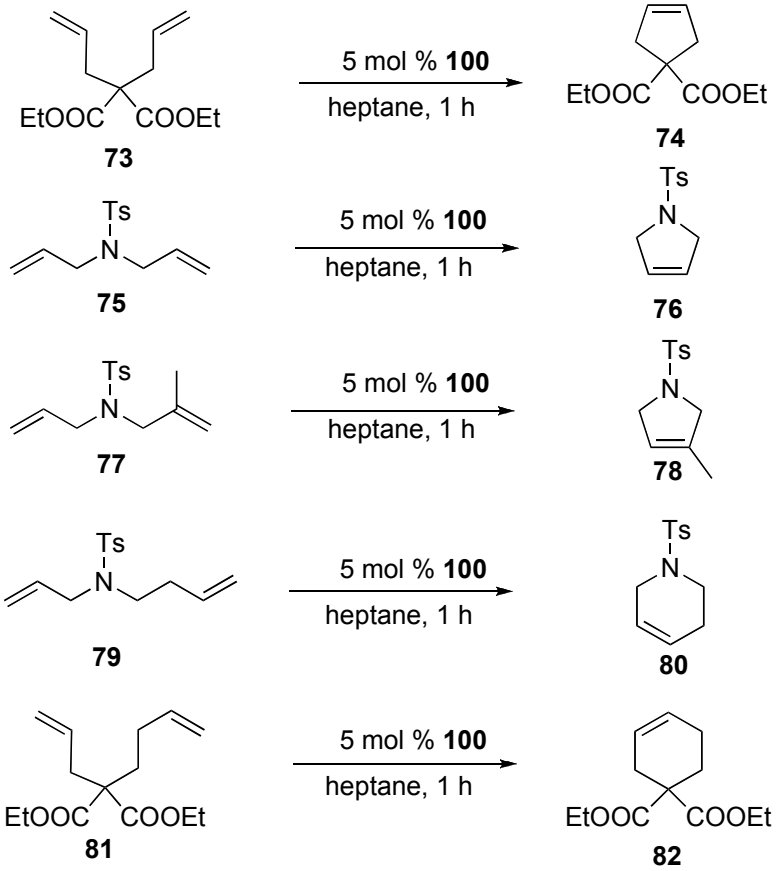
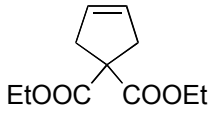
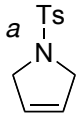
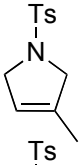
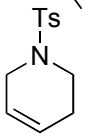
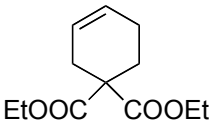


Table 3. Ring-closing metathesis reactions with catalyst **100**.

product	cycle 1	cycle 2	cycle 3	cycle 4	cycle 5
	60%	75%	85%	94%	94%
	72%	81%	99%	99%	99%
	67%	75%	93%	99%	99%
	59%	76%	84%	93%	93%
	62%	71%	97%	99%	99%

Yields in cycles 1-5 are for isolated products in 1 h, 0.5-mmol scale reactions and increase cycle to cycle because of saturation of the catalyst-containing heptane phase by products. [a]20 cycles (average yield of 97%/cycle) were carried out with reaction times of 2 h in the 12^{th}-13^{th} cycles, 4 h in 14^{th}-18^{th} cycles and 8 h in 19^{th}-20^{th} cycles.

Ruthenium complexes like **100** are structurally analogous to the Ru complex **101** previously used in ring-closing metathesis.[136] However, unlike **101**, **100** could be recycled in up to twenty cycles to convert a variety of 1,6-dienes and 1,7-dienes into cyclic olefins at room temperature (Table 3). Recycling of **100** was accomplished in one of two ways. The first approach, used for ring-closing metathesis of dienes **73** and **81**,

used heptane as a solvent, extracting product afterwards with CH_3CN. In this approach, the less dense heptane phase containing **100** was reused by simply adding fresh substrate. Products **74** and **82** were then isolated by removal of the CH_3CN.

Scheme 7. The mechanism of the ring-closing metathesis reaction with **72** as a ruthenium source versus **100** as a ruthenium source for the formation of the actual catalyst intermediates in the ring-closing metathesis catalytic cycle.

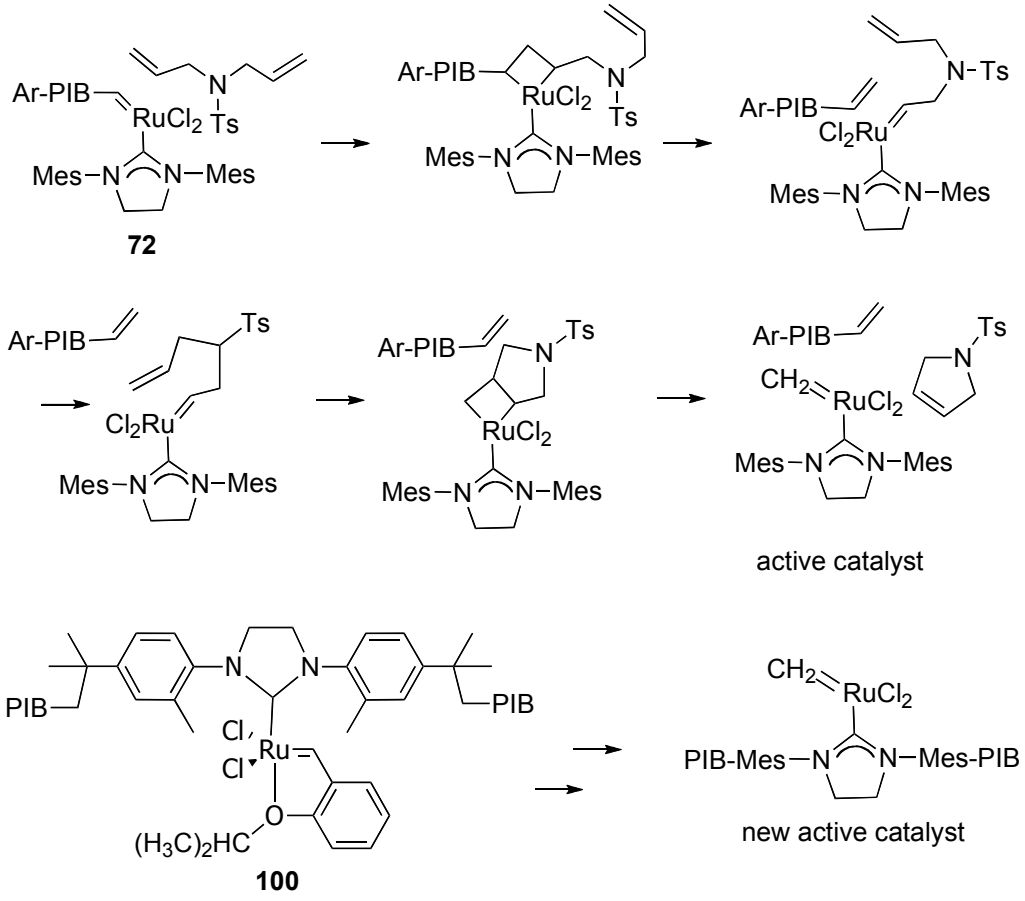


Figure 9. The comparison between two RCM products of catalyst **72** (left) and catalyst **100** (right).

While most catalyst recovery schemes focus on catalyst separation, the solubility of **100** in heptane and the low solubility of many organic compounds in heptane allowed us to use another recycling scheme for substrates **75**, **77**, and **79**. In these cases, starting materials were soluble in a heptane solution of the catalyst, but the products precipitated from solution and separated themselves from **100**. In these cases, products **76**, **78**, and **80** were recovered by simple filtration and recycling only required adding a fresh substrate to the recovered solution containing **100**.

The recyclability/recoverability of **100** was evaluated by ICP-MS analysis. Samples of product **76** from the first, second, fifth, and fourteenth cycles were digested in concentrated nitric acid and following by sulfuric acid. The ICP-MS results showed that only 0.28-0.54% of the starting Ru was in the product phase. This level of leaching of Ru is comparable to that seen for a water soluble PEG-supported SIMes.[171] Moreover, the metal leaching is ca. 10-fold less than that observed for a Ru catalysts that used a PIB-bound benzylidene ligand (**72**) – chemistry in Chapter III of this dissertation that depended on a 'boomerang' reaction for catalyst recovery (Scheme 7).[150]

As noted above and as shown in Scheme 7, both PIB-bound ruthenium **72** and **100** is only a precatalyst. The actual active catalyst is a Ru-methylidene. Thus, the attachment of polymer to ruthenium through a benzylidene ligand does not insure that the polymer support is attached to the ruthenium during the catalysis process. The alternative approach shown in this chapter to the synthesis of the ruthenium complex **100** addresses this problem by attaching PIB onto the NHC ligand. This strategy improved the recycling efficiency of the PIB-bound ruthenium catalyst greatly. With the PIB-bound ruthenium **100**, the PIB support will stay attached to the actual catalyst throughout the catalytic cycle. This reduces the likelihood of ruthenium metal leaching into the product phase. Visual evidence of reduced ruthenium leaching can be seen in Figure 9. The RCM product of catalyst **100** is water white in comparison to the colored product of catalyst **72**.

Conclusions

The studies in this chapter show that terminally vinyl-functionalized polyisobutylene oligomers can be easily transformed into end-functionalized PIB-bound *N*-heterocyclic carbenes, which can be used as ligands for 2nd generation Hoveyda-Grubbs catalyst. The success of each step in the synthesis of heptane-soluble catalyst **100** can be easily monitored by conventional NMR spectroscopy as was true in the synthesis of the PIB-bound ruthenium catalyst **72** discussed in Chapter III. Catalyst **100** can be used as a solution in heptane and recycled as a heptane solution after a gravity-based extraction using a heptane-immiscible polar solvent such as acetonitrile to extract

products. The alternative method of separations involves the precipitation of products from the heptane solution of the catalyst. These strategies are identical to those of catalyst **72** in Chapter III. The ICP-MS results and the visual evidence (Figure 9) prove that PIB-bound ruthenium **100** can be recovered and recycled much more efficiently than the previous PIB-bound ruthenium **72**.

CHAPTER V

CONCLUSIONS

In summary, the studies in this dissertation show that polyisobutylene oligomers are excellent nonpolar phase tags for chromophoric salen Cr(III) complexes and Hoveyda-Grubbs 2nd generation catalysts. This phase tag facilitates separation of catalysts from products as shown in both ring opening of epoxides, polymerization of polycarbonate, and ring-closing metathesis. This separation can be visually observed by the difference in color for the product polymer or product polymer phase as shown in chapters II, III, and IV. The result from ICP-MS data also indicated only minimal amount of catalyst leaching. The syntheses of PIB- bound ligands and catalysts are straightforward. The synthetic products and the intermediates in the ligand synthesis can all be readily analyzed spectroscopically. The activity of the PIB-supported catalysts is shown to be analogous to that of other soluble polymer supported catalysts or their non-supported analogs. The PIB-bound catalysts can be separated from products by a latent biphasic, liquid/liquid extractions, or product self-separation systems. The recovered PIB-bound catalysts can then be recycled multiple times. PIB enables the use of "Green" chemistry principles to utilized as ways to simplify catalyst, reagent, and product recovery.

CHAPTER VI

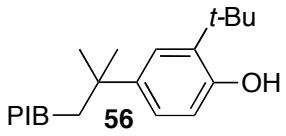
EXPERIMENTAL SECTION

Materials. Acetonitrile, heptane, dimethylformamide, ethanol, dichloromethane, and toluene were purchased from EMD and used as received. All chemicals were purchased from Sigma-Aldrich and used as received. Polyisobutylene was a gift from BASF.

Instrumentation. The ^{1}H-NMR spectra were recorded on an Inova 500MHz spectrometer operating at 499.95 MHz and Inova 300 MHz spectrometer operating at 299.91 MHz. ^{13}C-NMR spectra were recorded on an Inova 500 MHz spectrometer operating at 125.719 MHz and Inova 300 MHz spectrometer operating at 75.41 MHz. Chemical shifts were reported in parts per million (δ) relative to residual proton resonances in the deuterated chloroform ($CDCl_3$). Coupling constants (*J* values) were reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), and m (multiplet). UV-Vis spectra were obtained using a Varian Cary 100 spectrometer. IR spectra were obtained using a Bruker Tensor 27 FT-IR. ICP-MS data were obtained using a Perkin Elmer DRC II instrument. The polycarbonate polymerization carried out in a Parr® autoclave modified with a SiComp attenuated total reflectance window to allow for *in situ* infrared measurements by an ASI® ReactIR 1000**.**

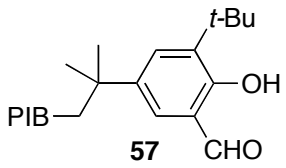
General Experimental Procedure. All reactions were carried out under an inert atmosphere unless otherwise noted. Products were isolated simply by evaporation of solvent without chromatography.

Synthesis of Polyisobutylene Supported Salen Cr(III) Complex



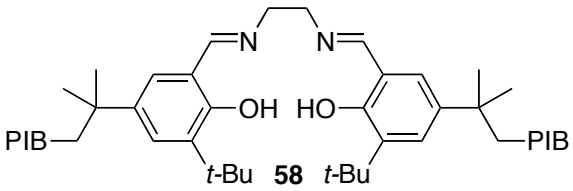
56

2-*tert*-butyl-4-(polyisobutyl)phenol: A mixture of 15 g (100 mmol) of 2-*tert*-butyl phenol, 8.9 g (8.9 mmol) of polyisobutylene (Glissopal® 1000), and 1.05 g (10.7 mmol) of concentrated sulfuric acid in 200 mL of dichloromethane was stirred for 3 days at room temperature. The solvent was removed under reduced pressure and then 250 mL of hexane was added to the viscous residue. The hexane solution was washed with 150 mL of dimethylformamide three times, then 150 mL of 90% ethanol/water three times. The hexane phase was dried over sodium sulfate. The solvent was removed under reduced pressure resulted in light yellow viscous residue. Yield was 85%. ^{1}H-NMR (300 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 6.6 (d, J = 7.75 Hz, 1H), 7.05 (m, 1H), and 7.3 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 151.83, 142.07, 135.04, 125.42, 124.53, 115.91, multiple peaks between 58 - 60, and 22 - 39.



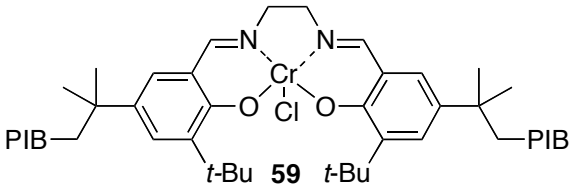
57

2-hydroxy-4-*tert*-butyl-5-(polyisobutyl)benzaldehyde: A mixture of 3.42 g (3.13 mmol) of 2-*tert*-butyl-4-(polyisobutyl)phenol and 0.58 mL (5 mmol) of 2,6-lutidine in 40 mL of toluene was stirred under room temperature for 30 min. A solution of $SnCl_4$ (0.15 mL, 1.25 mmol) in 10 mL of toluene was added slowly to the reaction. The reaction was then stirred under room temperature for 1 h at which point 0.56 g (18.78 mmol) of paraformaldehyde was added to reaction. The reaction was heated for 12 h at 100 ^{o}C. After the reaction mixture cooled to room temperature, it was acidified to pH 2.0 with 2 M HCl. The organic layer was separated, the solvent was removed under reduced pressure, and then 250 mL of hexane was added to the viscous residue. The hexane solution was washed first with 150 mL of dimethylformamide three times and then with 150 mL of 90% ethanol/water three times. The hexane phase was dried over sodium sulfate. The solvent was removed under reduced pressure to yield a light yellow viscous residue. The yield was 76%. ^{1}H-NMR (300 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 7.32 (s, 1H), 7.57 (s, 1H), 9.9 (s, 1H), and 11.62 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 197.55, 159.30, 140.89, 137.40, 133.20, 128.74, 120.19, multiple peaks between 58 - 60, and 22 - 39.



58

PIB supported salen(ethylene diamine): A mixture of 3.0 g (2.6 mmol) of 2-hydroxy-4-*tert*-butyl-5-(polyisobutyl)benzaldehyde, 0.08 g (1.3 mmol) of ethylenediamine, and catalytic amount of PTSA in 30 mL of toluene was refluxed overnight with Dean-Stark trap. The solvent was removed under reduced pressure and then 150 mL of hexane was added to the viscous residue. The hexane solution was washed with 100 mL of dimethylformamide three times, then 100 mL of 90% ethanol/water three times. The hexane phase was dried over sodium sulfate. The solvent was removed under reduced pressure resulted in yellow viscous residue. Yield was 99%. ^{1}H-NMR (300 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 280H), 1.8 (s, 4H), 3.95 (s, 4H), 7.05 (s, 1H), 7.40 (s, 1H), and 8.43 (s, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$), δ: 168.10, 158.20, 139.80, 136.50, 128.40, 127.70, 118.20, multiple peaks between 58 - 60, and 22 - 39.



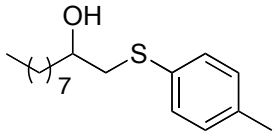
59

PIB supported salen Cr(III) complex: A mixture of 6.62 g (2.78 mmol) of salen(ethylene diamine)-supported PIB and 0.374 g (3.05 mmol) of $CrCl_2$ in 30 mL of

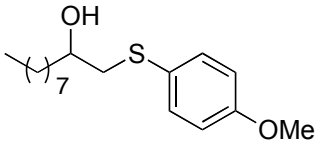
THF was put under N_2 atmosphere. The reaction was stirred under room temperature for 24 h and then 24 h in open air. The solvent was removed under reduced pressure and then 150 mL of hexane was added to the viscous residue. The hexane solution was washed with a solution of NH_4Cl three times, and then washed with 100 mL of brine. The hexane phase was dried over sodium sulfate. The solvent was removed under reduced pressure resulted in dark brown viscous residue. Yield was 65%. IR (neat): cm^{-1} 1625 (m), 1535 (s), 1467 (s), 1394 (s), 1364 (s), and 1235 (m). UV-visible spectroscopy (λ_{max} = 350 nm, $\varepsilon = 4514\ M^{-1}cm^{-1}$).

General Procedure for Epoxide Ring Opening Reactions

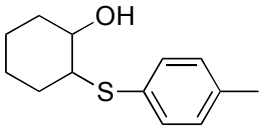
A mixture of 2 mmol of epoxide, 2 mmol of thiols, and 0.05 g (0.02 mmol) of catalyst were dissolved in 3 mL heptane and 3 mL EtOH. The reaction mixture was put under N_2 atmosphere and stirred over 24 h. Approximately 0.3 mL of water was added to the reaction mixture to form a biphasic layer. The EtOH layer was taken and diluted with 30 mL of diethyl ether. The diethyl ether solution was washed with 20 mL of water 3 times, then washed with 20 mL of brine and dried over sodium sulfate. The solvent was removed under reduce pressure.



^{1}H-NMR (300 MHz, $CDCl_3$), δ: 0.9 (t, *J* = 6.91 Hz, 3H), 1.2-1.6 (m, 14H), 2.35 (s, 3H), 2.8 (m, 1H), 3.1 (m, 1H), 3.6 (m, 1H), 7.1 (d, *J* = 8.60 Hz, 2H), and 7.3 (d, *J* = 8.60 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$), δ: 137, 131, 130, 128, 69, 43, 36, 29.4, 29.2, 17.5, 23, 21, and 14.

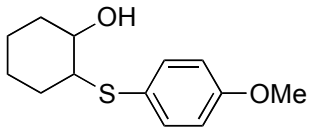


^{1}H-NMR (300 MHz, $CDCl_3$), δ: 0.9 (t, *J* = 7.04 Hz, 3H), 1.2-1.6 (m, 14H), 2.78 (mm, 1H), 3.05 (m, 1H), 3.8 (s, 3H), 6.83 (d, *J* = 8.47 Hz, 2H), and 7.4 (d, *J* = 8.47 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$), δ: 159.7, 134, 125.5, 115, 69.2, 55.8, 45, 36.5, 32, 29.6, 29.3, 27.5, 26, 23, and 14.3.

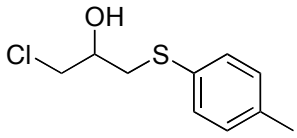


^{1}H-NMR (300 MHz, $CDCl_3$), δ: 1.3 (m, 4H), 1.7 (m, 2H), 2.1 (m, 2H), 2.37 (s, 3H), 2.7, (m, 1H), 3.3, (m, 1H), 7.1 (d, *J* = 7.83 Hz, 2H), and 7.4 (d, *J* = 7.83 Hz, 2H). ^{13}C-NMR

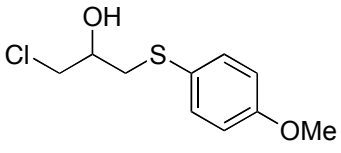
(75 MHz, $CDCl_3$), δ: 138.4, 134.8, 130, 128, 72, 56.8, 34, 32.7, 26.4, 24.5, and 21.4.



^{1}H-NMR (300 MHz, $CDCl_3$), δ: 1.25 (m, 4H), 1.75 (m, 2H), 2.1 (m, 2H), 2.6 (m, 1H), 3.23, (m, 1H), 3.8, (s, 3H), 6.85 (d, J = 8.82 Hz, 2H), and 7.42 (d, J = 8.82 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$), δ: 160, 137.3, 122, 114.7, 71.6, 57, 55.6, 33.9, 32.5, 26.4, and 24.5.



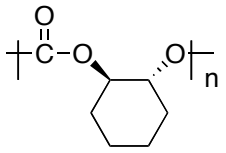
^{1}H-NMR (300 MHz, $CDCl_3$), δ: 2.3 (s, 3H), 2.95 (m, 1H), 3.03 (m, 1H), 3.58 (m, 1H), 3.77 (m, 1H), 7.1 (d, J = 8.29 Hz, 2H), and 7.3 (d, J = 8.29 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$), δ: 137.48, 135.2, 131.3, 130.2, 69.8, 65.4, 38.9, and 21.3.



^{1}H-NMR (300 MHz, $CDCl_3$), δ: 2.9 (m, 1H), 3.03 (m, 1H), 3.6 (m, 1H), 3.77 (m, 1H),

3.82 (s, 3H), 6.9 (d, J = 8.51 Hz, 2H), and 7.4 (d, J = 8.51 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$), δ: 134.2, 132.9, 115.06, 114.8, 69.74, 65.4, 55.6, and 40.2.

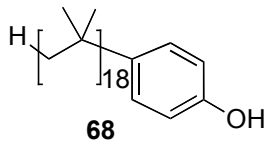
Polymerization of polycarbonate by PIB supported salen Cr(III) complex



210 mg (approx. 0.085 mmol) of PIB supported salen Cr(III) complex (**59**) and 37 mg (0.064 mmol) of PPNCl (PPNCl = Bis(triphenylphosphoranylidene)ammonium chloride) were weighed into a glass vial in a controlled atmosphere glove box and sealed with a septum. The catalyst/cocatalyst mixture was then dissolved in 20 mL of CH_2Cl_2 and stirred for 30 minutes. After removal of the solvent via vacuum, the activated catalyst was dissolved in 10 mL of cyclohexene oxide (CHO). The catalyst solution was then loaded via cannula into a 300 mL Parr® reactor that had been previously dried via heating overnight at 80 °C. The vial was rinsed with an additional 10 mL of CHO and added to the reactor. The reaction vessel was pressurized to 35 bar CO_2 and heated to 80 °C for 4 h. Upon completion of the reaction, the vessel was cooled and the CO_2 vented. The resulting polymer solution was dissolved in CH_3CN (for biphasic separation) or CH_2Cl_2 (for acidified methanol separation) depending on the chosen method of purification. Alternatively, the reaction was carried out in a Parr® autoclave modified with a SiComp attenuated total reflectance window to allow for *in*

situ infrared measurements using an ASI® ReactIR 1000. Analogously, the activated catalyst was dissolved in 10 mL of CHO and loaded into the reaction vessel at 80 °C at which time a single 128 scan background spectrum was collected. The vial was then rinsed with 10 mL of CHO and loaded into the autoclave. After pressurization with 35 bar CO_2, a single 128 scan spectrum was collected every 3 minutes for 4 to 6 h. Reaction progress was followed by monitoring the absorbance of the polycarbonate (1750 cm^{-1}) and cyclic carbonate (~ 1825 cm^{-1}) versus time. Upon completion of the reaction, the reaction vessel was cooled and the CO_2 vented followed by dissolution of the polymer catalyst mixture in 50 mL of CH_3CN. Approximately 1 mL of concentrated HCl was added to the mixture and stirred for 3 h, the solution was concentrated and precipitated in hexane to yield white powdery residue.

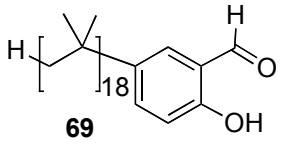
Synthesis of PIB Supported Grubbs-Hoveyda 2nd Generation Catalyst



68

4-(polyisobutyl)phenol: A mixture of 16.75 g (178 mmol) of phenol, 8.9 g (8.9 mmol) of polyisobutylene (Glissopal® 1000), and 1.05 g (10.7 mmol) of concentrated sulfuric acid in 200 mL of dichloromethane was stirred for 3 days at room temperature. The solvent was removed under reduced pressure and then 250 mL of hexane was added to the viscous residue. The hexane solution was washed with 150 mL of

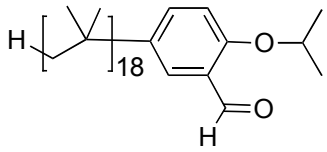
dimethylformamide three times, then 150 mL of 90% ethanol/water three times. The hexane phase was dried over sodium sulfate. The solvent was removed under reduced pressure resulted in light yellow viscous residue. Yield was 70%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 6.75 (d, J = 8.79 Hz, 2H), and 7.23 (d, J = 8.79 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 153.19, 142.99, 127.52, 114.75, multiple peaks between 58 - 60, 38 - 38.5, and 30.75 - 33.



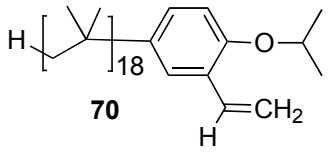
69

2-hydroxy-5-(polyisobutyl)benzaldehyde: A mixture of 3.42 g (3.13 mmol) of 4-(polyisobutyl)phenol and 0.58 mL (5 mmol) of 2,6-lutidine in 40 mL of toluene was stirred under room temperature for 30 minutes. A solution of $SnCl_4$ (0.15 mL, 1.25 mmol) in 10 mL of toluene was added slowly to the reaction. The reaction was stirred under room temperature of 1 h and then 0.56 g (18.78 mmol) of paraformaldehyde was added to reaction. The reaction was heated for 12 h at 100 ^{o}C. After the reaction mixture cooled to room temperature, it was acidified to pH 2.0 with 2 M HCl. The organic layer was separated and solvent was removed under reduced pressure and then 250 mL of hexane was added to the viscous residue. The hexane solution was washed with 150 mL of dimethylformamide three times, then 150 mL of 90% ethanol/water three times. The hexane phase was dried over sodium sulfate. The solvent was removed under reduced pressure resulted in light yellow viscous residue. Yield was 76%. ^{1}H-

NMR (500 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 6.94 (d, *J* = 8.54 Hz, 1H), 7.48 (m, 1H), 7.57 (dd, *J* = 2.44, 8.54 Hz, 1H), 9.9 (s, 1H), and 10.88 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 197.07, 159.65, 142.40, 135.74, 130.73, 120.21, 117.24, multiple peaks between 58 - 60, 38 - 38.5, and 30.75 - 33.



2-isoproproxy-5-(polyisobutyl)benzaldehyde: A mixture of 2.5 g (2.25 mmol) of 2-hydroxy-5-(polyisobutyl)benzaldehyde and 0.425 g (2.5 mmol) of isopropyl iodide in 10 mL of dimethylformamide and 10 mL of heptane was heated to 80 ^{o}C overnight, then cooled to room temperature and 50 mL of hexane was added to the solution. The hexane solution was washed with 30 mL of dimethylformamide three times, then 30 mL of 90% ethanol/water three times. The hexane phase was dried over sodium sulfate. The solvent was removed under reduced pressure resulted in light yellow viscous residue. Yield was 76%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 4.66 (m, 1H), 6.92 (d, *J* = 8.79 Hz, 1H), 7.53 (dd, *J* = 2.69, 8.79 Hz, 1H), 7.82 (d, *J* = 2.69 Hz, 1H), and 10.49 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 190.68, 158.75, 142.92, 134.06, 125.63, 125.21, 113.83, 71.34, multiple peaks between 58 - 60, 38 - 38.5, and 30.75 - 33.



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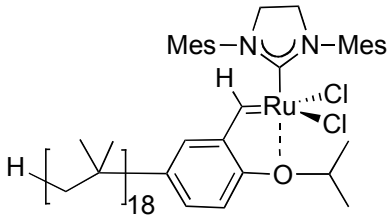
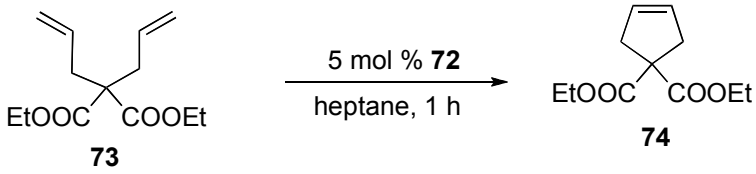
1-isoproproxy-4-(polyisobutyl)-2-vinylbenzene: 3.21 g (7.96 mmol) of methyltriphenylphosphonium iodide was added to 30 mL of THF, then 5 mL of 1.6 M ^{n}BuLi was added slowly to the solution and let it stirred for 2 h. The solution turned bright yellow. The solution was cooled to -78 ^{o}C and a solution of 4.6g (3.98 mmol) of 2-isoproproxy-5-(polyisobutyl)benzaldehyde ether in THF was added slowly to the mixture. The reaction was stirred overnight. The solvent was removed under reduced pressure and then 100 mL of hexane was added to the viscous residue. The hexane solution was washed with 75 mL of dimethylformamide three times, then 75 mL of 90% ethanol/water three times. The hexane phase was dried over sodium sulfate. The solvent was removed under reduced pressure resulted in light yellow viscous residue. Yield was 80%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8 - 1.6 (m, 140H), 1.8 (s, 2H), 4.51 (m, 1H), 5.23 (dd, *J* = 1.46, 11.10 Hz, 1H), 5.73 (dd, *J* = 1.46, 17.70 Hz, 1H), 6.81 (d, *J* = 8.55 Hz, 1H), 7.07 (dd, *J* = 11.10, 17.70 Hz, 1H), 7.19 (dd, *J* = 2.45, 8.55 Hz, 1H), and 7.46 (d, *J* = 2.45 Hz 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 153.13, 142.54, 132.96, 127.11, 126.71, 124.62, 113.98, 113.67, 71.11, multiple peaks between 58 - 60, 38 - 38.5, and 30.75 - 33.



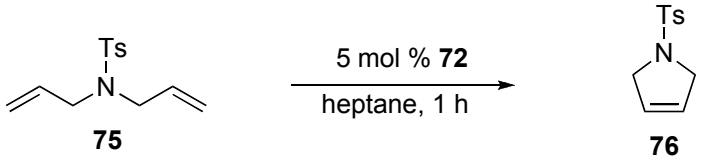
72

PIB supported Grubbs-Hoveyda 2nd generation catalyst: A mixture of 2 g (1.72 mmol) of 1-isoproproxy-4-(polyisobutyl)-2-vinylbenzene, 0.12 g (1.21 mmol) of CuCl, and 0.73 g (0.86 mmol) of 2nd generation Grubbs catalyst in dichloromethane was stirred at 40 ^{o}C overnight. The solution turned from red to green as the reaction progressed. The solvent was removed under reduced pressure and purified with column chromatography (2:1 hexane:dichloromethane) resulted in dark green viscous residue. The solvent was removed under reduced pressure resulted in light yellow viscous residue. Yield was 87%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8 -1 .6 (m, 140H), 1.8 (s, 2H), 2.42 - 2.49 (m, 18H), 4.20 (s, 4 H), 4.87 (m, 1H), 6.71 (d, *J* = 8.92 Hz, 1H), 6.87 (d, *J* = 1.94 Hz, 1H), 7.09 (s, 4H), 7.48 (dd, *J* = 1.94, 8.92 Hz, 1H), and 16.32 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 298.35 (m), 212.65, 150.40, 145.13, 145.11, 138.97, 129.58, 129.57, 129.55, 127.55, 120.59, 112.25, 74.81, multiple peaks between 58 - 60, 38 - 38.5, and 30.75 - 33. λ_{max} = 591 nm. IR (KBr): 2954 (br), 2870 (br), 1729 (w), 1612 (w), 1592 (w), 1488 (s), 1455 (m), 1391 (s), 1367 (s), 1297 (m), 1267 (s), 1232 (s), 1139 (m), 1108 (m), 1037 (m), 927 (m), 854 (m), 815 (m), 739 (S), 704 (m), 649 (m), 621 (w), 580 (m)

Procedures and Characterization for Ring Closing Metathesis Reaction and ROMP

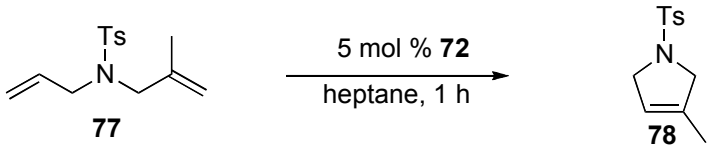


A mixture of 120 mg (0.5 mmol) substrate **73** and 40 mg (0.025 mmol) of catalyst **72** were dissolved in 5 mL of heptane. The reaction was stirred for 1 h. Once the reaction was completed, 3 mL of acetonitrile was added to the reaction mixture and stirred vigorously. After both phase of the solvent is separated, the acetonitrile layer was taken out. The solvent was removed under reduced pressure to yield compound **74**. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 1.24 (t, J = 7.33 Hz, 6H), 3.0 (s, 4H), 4.19 (q, J = 7.33 Hz, 4H), and 5.60 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 172.49, 128.05, 61.76, 59.07, 41.08, and 14.27.



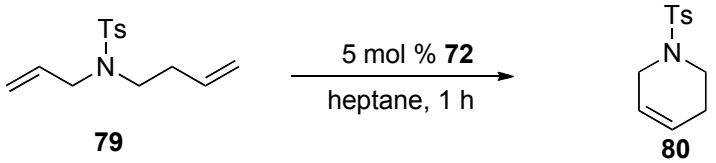
A mixture of 125 mg (0.5 mmol) substrate **75** and 40 mg (0.025 mmol) of catalyst **72** were dissolved in 5 mL of heptane. The reaction was stirred for 1 h. Once the reaction was completed, substrate **76** precipitated out of solution; therefore it was filtered out and dried under reduced pressure. The heptane layer was recycled in the subsequent

reactions. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 2.44 (s, 3H), 4.13 (s, 4H), 5.66 (s, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), and 7.73 (d, *J* = 8.3 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 143.68, 134.53, 130.0, 127.67, 125.70, 55.08, and 21.78. MP range = 123.2 - 126.5 ^{o}C



77 **78**

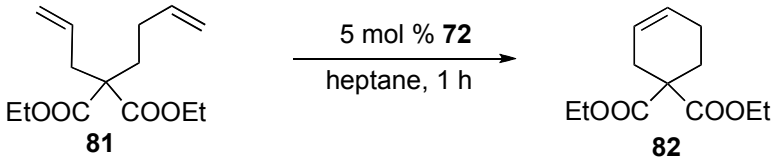
A mixture of 132 mg (0.5 mmol) substrate **77** and 40 mg (0.025 mmol) of catalyst **72** were dissolved in 5 mL of heptane. The reaction was stirred for 1 h. Once the reaction was completed, substrate **78** precipitated out of solution; therefore it was filtered out and dried under reduced pressure. The heptane layer was recycled in the subsequent reactions. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 1.66 (s, 3H), 2.43 (s, 3H), 3.97 (m, 2H), 4.07 (m, 2H), 5.25 (m, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), and 7.72 (d, *J* = 8.2 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 143.58, 135.31, 129.97, 127.70, 119.32, 117.84, 57.92, 55.37, 21.78, and 14.32. MP range = 100.8 - 101.8 ^{o}C



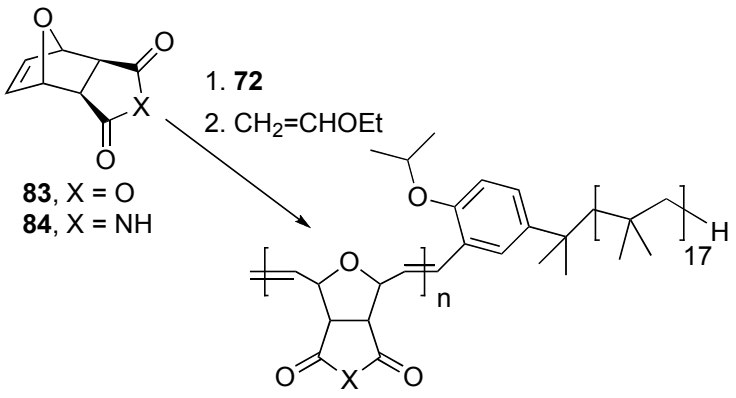
79 **80**

A mixture of 132 mg (0.5 mmol) substrate **79** and 40 mg (0.025 mmol) of catalyst **72** were dissolved in 5 mL of heptane. The reaction was stirred for 1 h. Once the reaction

was completed, substrate **80** precipitated out of solution; therefore it was filtered out and dried under reduced pressure. The heptane layer was recycled in the subsequent reactions. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 2.24 (m, 2H), 2.45 (s, 3H), 3.19 (t, J = 5.61 Hz, 2H), 3.59 (m, 2H), 5.63 (m, 1H), 5.77 (m, 1H), 7.34 (d, J = 8.3 Hz, 2H), and 7.70 (d, J = 8.3 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 143.73, 133.62, 129.86, 127.95, 125.31, 123.0, 45.02, 42.88, 25.51, and 21.77. MP range = 99.7 - 102.2 ^{o}C.



A mixture of 127 mg (0.5 mmol) substrate **81** and 40 mg (0.025 mmol) of catalyst **72** were dissolved in 5 mL of heptane. The reaction was stirred for 1 h. Once the reaction was completed, 3 mL of acetonitrile was added to the reaction mixture and stirred vigorously. After both phase of the solvent is separated, the acetonitrile layer was taken out. The heptane layer was recycled in the subsequent reactions. The solvent was removed under reduced pressure to yield compound **82**. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 1.25 (m, 6H), 2.12 (m, 4H), 2.56 (s, 2H), 4.19 (m, 4H), and 5.68 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 171.84, 126.31, 124.24, 61.49, 53.16, 30.64, 27.57, 22.54, and 14.27.



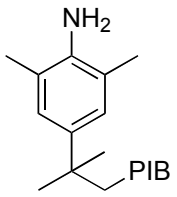
The catalyst (20 mg, 0.012 mmol) was dissolved in 2 mL of THF. It was then added dropwise to a THF solution (5 mL) of the monomer (**83**: 60.9 mg, 0.37 mmol, 30 equiv., **84**: 60.5 mg, 0.37 mmol, 30 equiv.), and the reaction was stirred at room temperature. The color of the solution turned from green to light grey in less than 2 minutes. The solution was stirred for 20 minutes, and then ethyl vinyl ether (0.4 mL, 600 equiv.) was added and stirring continued for 15 minutes. The polymerization solution was then poured into methanol (100 mL) while stirring to give a light greenish solid that was collected and dried under vacuum.

Ruthenium Analysis Procedure

To a 20 mL vial, 27.3 mg of sample and 4 g of concentrated nitric acid were added. The mixture was heated up to 120 ^{o}C until homogenized and then 4 g of concentrated sulfuric acid was added to the solution and leave it at room temperature for 24 h. The concentrated acidic aqueous solution was then transferred to a 50 mL plastic bottle and diluted to 50 mL with 1% nitric acid solution. 0.2063 g of the solution was further

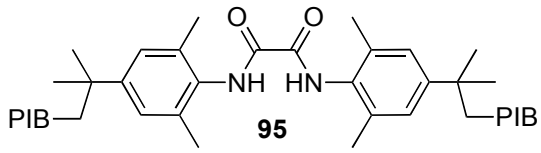
diluted to 50 mL again with 1% nitric acid. Then, the diluted sample solution was analyzed with ICP-MS.

Synthesis of PIB Supported NHC, Grubbs-Hoveyda 2nd Generation Catalyst



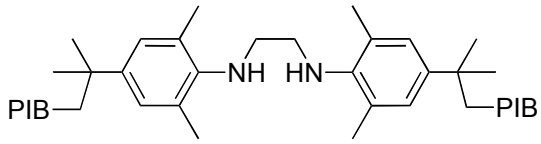
94

2,6-Dimethyl-4-(polyisobutyl)aniline: A mixture of 12.4 g (102 mmol) of 2,6-dimethylaniline, 10.15 g (10.15 mmol) of polyisobutylene (Glissopal® 1000), and 4.4 g (33 mmol) of aluminum trichloride was stirred for 3 d at 220 ^{o}C in a pressure vessel. After 3 d, the deep purple solution reaction was cooled to approximately 100 ^{o}C and added to 200 mL of hexane. The solution so formed was washed with 150 mL of dimethylformamide three times and then with 150 mL of 90% ethanol/water three times. After drying over sodium sulfate, the solvent was removed under reduced pressure and the product was purified by column chromatography (eluted first with hexane and then with dichloromethane). Solvent removal afforded the product as a light yellow viscous residue. The yield was 65%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8-1.6 (m, 140H), 1.8 (s, 2H), 2.19 (s, 6H), 3.45 (s, 2H), and 6.92 (s, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 140.27, 140.06, 126.30, 121.28, multiple peaks between 58 - 60, 30 - 40, and 18.26.



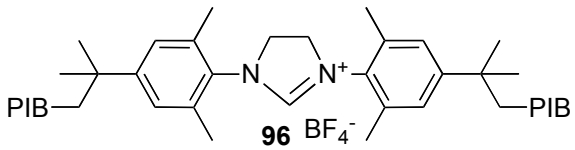
95

***N,N'*-Bis(2,6-dimethyl-4-(polyisobutyl) phenyl)oxalamide:** A mixture of 6 g (5.35 mmol) of 2,6-dimethyl-4-(polyisobutyl)aniline and 0.64 g (6.3 mmol) of triethylamine in 30 mL of dichloromethane was cooled to 0 ^{o}C. A solution of oxalyl chloride (0.4 g, 3.15 mmol) in 5 mL of dichloromethane was added slowly to the reaction. The reaction was then stirred overnight. The solvent was removed under reduced pressure and added to 150 mL of hexane. The hexane solution was washed with 100 mL of 90% ethanol/water three times. The hexane phase was dried over sodium sulfate and shaken with 6 g of acid Amberlyst XN-1010 for 4 h, and then the resin was removed by filtration. The solvent was removed under reduced pressure to yield a light yellow viscous residue. The yield was 88%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8-1.6 (m, 280H), 1.82 (s, 4H), 2.28 (s, 12H), 7.11 (s, 2H), and 8.82 (s, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 158.25, 150.15, 134.05, 129.30, 126.20, multiple peaks between 58 - 60, 30 - 40, and 18.26.



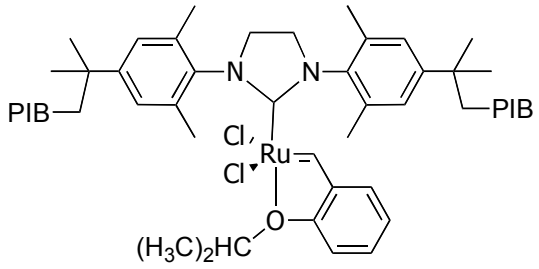
***N,N'*-Bis(2,6-dimethyl-4-(polyisobutyl) phenyl) ethane-1,2-diamine:** A 6.34 g (2.76 mmol) sample of *N,N'*-bis(2,6-dimethyl-4-(polyisobutyl)phenyl)oxalamide was

dissolved in 30 mL of toluene, then 1.83 mL (18.67 mmol) of BH_3-SMe_2 was added to the solution. The solution turned from yellow to almost colorless. The reaction was heated at 90 ^oC overnight. The solvent was removed under reduced pressure and purified by column chromatography (10:1/hexane:dichloromethane). Solvent removal afforded a light yellow viscous residue. The yield was 61%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8-1.6 (m, 280H), 1.77 (s, 4H), 2.30 (s, 12H), 3.17 (s, 4H), and 6.97 (s, 4H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 144.18, 143.23, 128.92, 126.96, 49.30, multiple peaks between 58 - 60, 30 - 40, and 18.26.



96

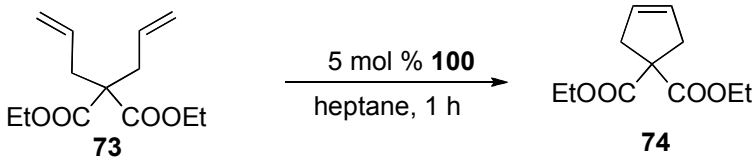
1,3-Bis(2,6-dimethyl-4-(polyisobutyl) phenyl)-4,5-dihydro-imidazolium tetrafluoro-borate: A 3.62 g (1.6 mmol) sample of *N*,*N'*-bis(2,6-dimethyl-4-(polyisobutyl)phenyl)ethane-1,2-diamine was dissolved in 10 mL of triethylorthoformate and followed by the addition of 230 mg (2.19 mmol) of ammonium tetrafluroborate and heated to 120 ^oC overnight. The solvent was removed under reduced pressure and purified by column chromatography (9:1/dichloromethane:methanol) resulted in a dark yellow viscous residue. The yield was 79%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8-1.6 (m, 280H), 1.85 (s, 4H), 2.42 (s, 12H), 4.65 (s, 4H), 7.17 (s, 4H), and 7.65 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 158.25, 154.11, 134.54, 129.84, 127.60, 52.37, multiple peaks between 58 - 60, 30 - 40, and 18.26.



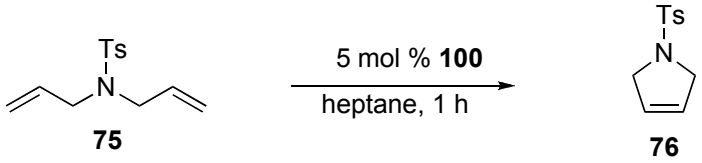
100

PIB supported Grubbs-Hoveyda 2nd generation catalyst: A mixture of 1.14 g (0.48 mmol) of 1,3-bis(2,6-dimethyl-4-(polyisobutyl)phenyl)-4,5-dihydro-imid-azolium tetrafluoroborate, 0.15 g (0.75 mmol) of KHMDS, 0.05 g (0.5 mmol) of CuCl and 0.36 g (0.57 mmol) of 1st generation Hoveyda-Grubbs catalyst was dissolved in 5 mL of toluene. The solution was heated to 100 ^{o}C for 3 h. Solvent was removed under reduced pressure and purified by column chromatography (dichloromethane) resulted in a dark green viscous residue. The yield was 60%. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 0.8-1.6 (m, 280H), 1.87 (s, 4H), 2.41 (b, 6H), 2.62 (b, 6H) 4.15 (s, 4H), 4.90 (m, 1H), 6.8 (m, 2H), 6.98 (m, 1H), 7.22 (b, 4H), 7.47 (m, 1H), and 16.67 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 297.23 (m), 211.19, 152.45, 152.43, 152.16, 145.44, 145.41, 139.21, 137.30, 129.69, 127.01, 126.53, 123.09, 122.42, 113.10, multiple peaks between 58 - 60, 30 - 40, and 21.62.

Procedures for Ring Closing Metathesis Reaction

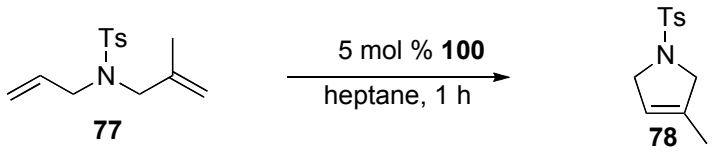


A mixture of 120 mg (0.5 mmol) of substrate **73** and 65 mg (0.025 mmol) of catalyst **100** were dissolved in 5 mL of heptane. After 1 h, the reaction was complete. At this point, 3 mL of acetonitrile was added to the reaction mixture. After vigorous stirring, the mixture was allowed to settle and the two phases were separated. The acetonitrile layer containing the product was dried under reduced pressure to yield compound **74**. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 1.24 (t, J = 7.33 Hz, 6H), 3.0 (s, 4H), 4.19 (q, J = 7.33 Hz, 4H), and 5.60 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 172.49, 128.05, 61.76, 59.07, 41.08, and 14.27.

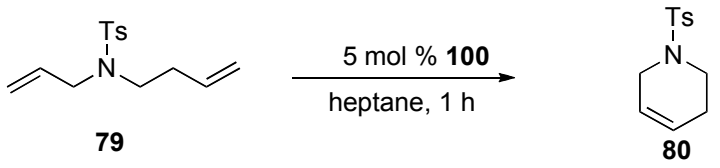


A mixture of 125 mg (0.5 mmol) of substrate **75** and 65 mg (0.025 mmol) of catalyst **100** were dissolved in 5 mL of heptane. The reaction was stirred for 1 h during which time the substrate **76** precipitated from solution. The catalyst solution was separated from the product precipitates by filtration for reuse in a subsequent reaction cycle. The isolated

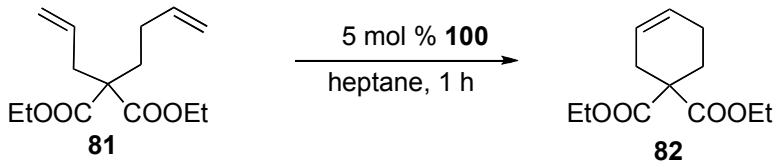
solid product was dried under reduced pressure. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 2.44 (s, 3H), 4.13 (s, 4H), 5.66 (s, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), and 7.73 (d, *J* = 8.3 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 143.68, 134.53, 130.0, 127.67, 125.70, 55.08, and 21.78. MP range = 123.2 - 126.5 ^{o}C



A mixture of 132 mg (0.5 mmol) of substrate **77** and 65 mg (0.025 mmol) of catalyst **100** were dissolved in 5 mL of heptane. The reaction was stirred for 1 h during which time the substrate **78** precipitated from solution. The catalyst solution was separated from the product precipitates by filtration for reuse in a subsequent reaction cycle. The isolated solid product was dried under reduced pressure. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 1.66 (s, 3H), 2.43 (s, 3H), 3.97 (m, 2H), 4.07 (m, 2H), 5.25 (m, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), and 7.72 (d, *J* = 8.2 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 143.58, 135.31, 129.97, 127.70, 119.32, 117.84, 57.92, 55.37, 21.78, and 14.32. MP range = 100.8 - 101.8 ^{o}C



A mixture of 132 mg (0.5 mmol) of substrate **79** and 65 mg (0.025 mmol) of catalyst **100** were dissolved in 5 mL of heptane. The reaction was stirred for 1 h during which time the substrate **80** precipitated from solution. The catalyst solution was separated from the product precipitates by filtration for reuse in a subsequent reaction cycle. The isolated solid product was dried under reduced pressure. ^{1}H-NMR (500 MHz, $CDCl_3$), δ: 2.24 (m, 2H), 2.45 (s, 3H), 3.19 (t, *J* = 5.61 Hz, 2H), 3.59 (m, 2H), 5.63 (m, 1H), 5.77 (m, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), and 7.70 (d, *J* = 8.3 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 143.73, 133.62, 129.86, 127.95, 125.31, 123.0, 45.02, 42.88, 25.51, and 21.77. MP range = 99.7 - 102.2 ^{o}C.



A mixture of 127 mg (0.5 mmol) of substrate **81** and 65 mg (0.025 mmol) of catalyst **100** were dissolved in 5 mL of heptane. After 1 h, the reaction was complete. At this point, 3 mL of acetonitrile was added to the reaction mixture. After vigorous stirring, the mixture was allowed to settle and the two phases were separated. The acetonitrile layer containing the product was dried under reduced pressure to yield compound **82**. ^{1}H-

NMR (500 MHz, $CDCl_3$), δ: 1.25 (m, 6H), 2.12 (m, 4H), 2.56 (s, 2H), 4.19 (m, 4H), and 5.68 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ: 171.84, 126.31, 124.24, 61.49, 53.16, 30.64, 27.57, 22.54, and 14.27.

Phase Selectivity Studies Procedure

The sample that was to be analyzed (0.12 mg) was dissolved in 12.0 mL of heptane. Then 2 mL of this heptane solution was added to 2 mL of polar solvent (acetonitrile, ethylene glycol diacetate, di(ethylene glycol) monomethyl ether or heptane-saturated DMF). The mixture was sealed and heated to 120 ^{o}C to generate a homogeneous solution (in the case of the heptane-acetonitrile system only partial miscibility occurred). The solution was cooled to room temperature and centrifuged for 1 h at 5 ^{o}C to produce a biphasic solution. Part of each phase was then analyzed by UV-Vis spectroscope. Another portion at each phase was used as a sample for metal analysis.

ICP-MS Digestion Procedure

The sample that was to be analyzed (3-25000 μg) and 4 g of concentrated nitric acid were added to a glass vial. The mixture was heated to 120 ^{o}C until most compounds were dissolved. At this point, 4 g of concentrated sulfuric acid was added to the solution at room temperature and heated to 120 ^{o}C until all of the compounds were dissolved. The solution was then allowed to stand at room temperature. At this point, the concentrated acidic aqueous solution was diluted with 1% nitric acid solution and the diluted sample solution was analyzed by ICP-MS.

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